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March, 1922

ADRENAL INSUFFICIENCY FROM THE VIEWPOINT OF THE CLINICIAN.*

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When the present journal, ENDOCRINOLOGY, was founded, it was deemed greatly to the interest of the newer branch of Medicine it represents, to insure impartiality in its dealings with all professional questions at issue. Hence the present article on a subject reviewed some months ago by Prof. G. N. Stewart (1) from the standpoint of the physiologist, in which he criticizes clinicians, our French and Italian colleagues in particular, because of their recognition of adrenal insufficiency as a morbid factor in many diseases. May there not be another side to this question?

Stewart's main contention is that the effects of removal of both adrenals in laboratory animals fails to reproduce a well marked syndrome of adrenal deficiency, and, therefore, that physicians are not justified in recognizing such a syndrome. Analysis of his paper suggests, however, that if with us, he worked in the clinical field, his conception of adrenal insufficiency would be different, for he would take cognizance as we

*Part of opening scientific address read before the Endocrinological Society of the City of New York, on January 6th, 1922.

do, of various pathological factors which partly explain the variations from the specific symptoms observed in *normal* animals after double adrenal extirpation. Again, he would realize that nothing in the pathological field corresponds with the sudden enucleation of the adrenals with all other organs and tissues in the body in normal health. Even adrenal apoplexy in which death occurs very soon after the onset of the acute symptoms, there exists a concomitant and causative toxemia with lesions in other organs which lead to hemorrhagic destruction of the adrenal tissues, already themselves the seat, in most cases, of organic lesions, cancerous, tuberculous, syphilitic, etc. Irrespective of any such fulminant and comparatively rare termination, the same local lesions, general toxemia, and its complications, hemolysis, autolysis and the active defensive reaction provoked, must be taken into account to interpret correctly the morbid process involved in adrenal insufficiency.

As recently explained by Sergent (2), what he and Bernard meant (1899) by adrenal insufficiency was a complete deficiency of all the functions of the adrenals (*"un déficit total des fonctions surrénales"*) including those of both cortex and medulla, after their destruction by local lesions, cancerous, tuberculous, etc. This cannot, however, rightly be termed adrenal insufficiency, but complete adrenal failure—a condition which should provoke in animals and men, and as it does usually, very grave symptoms usually followed by death—unless there exist reserves of adrenin to which I will presently refer.

What I have termed "hypoadrenia" (1907) is a condition, often observed late in acute febrile infections in which a reduction of chromaphil or medullary substance has been repeatedly demonstrated at autopsies. It occurs normally in old age, and has been shown histologically to be due to progressive vascular atrophy of the adrenals. It may also occur in infancy at the weaning period, when metabolic torpor fails to sustain organic functions; also after overexertion which likewise coincides with deficiency of the adrenal content in chromaphil substance. In all these there exist besides, systemic phenomena due to the pathogenic agent, toxins, endotoxins, wastes, the defensive reaction, lesions in other organs, including the nervous system, etc., which the trained endocrinologist takes into account. Stewart's lack of familiarity with these complicating factors is explained, doubt-

less, by the identity of hypoadrenia as a pathological entity which physiologists never witness. As the great Russian physiologist Pavloff so clearly urged twenty years ago, referring to the discovery of the gastric nerves by physicians: "The world of pathological phenomena is nothing but an endless series of the most different and unusual combinations of physiological combinations which never make their appearance in the normal course of life."

Again, clinicians would not endorse Stewart's statement, when referring to Addison's disease, that the majority of clinical writers still suppose that "it is the loss of epinephrin secretion of the medulla which is the important thing, although experimental physiology affords no basis for such a view." No present day clinician worthy of the name would think of "epinephrin secretion" as a sole factor in Addison's disease, being well aware of the fact that both the medulla and cortex may be the seat of lesions. Nor would a competent therapeutist administer epinephrin in such cases. Either the fresh gland, a glandular extract or the dried gland, all representing the whole gland must be used to expect beneficial results, as shown by a personal study of 120 reported cases. The single case of sudden death in a soldier reported by Boyd (3) is quoted by Stewart as "a safe conclusion that the medulla is not essential to life" because the man's adrenals were almost entirely converted into structureless masses" though he showed no signs of Addison's disease. A clinician would not consider this as a safe conclusion. Nearly two decades ago (4), I submitted ample evidence quite applicable to Boyd's soldier, to the effect that he could readily have fulfilled vicariously his adrenal function with his adrenals "almost entirely" destroyed functionally. Quoting my own words of 1903: "In four rats which survived bilateral adrenalectomy several months Boinet found three or four reddish organs round the kidneys structurally similar to the cortex of adrenals. . . . In the human being accessory suprarenal bodies have been found in the semilunar ganglion and in the midst of the solar plexus by Jaboulay and by Stilling. Gottschalk found accessory adrenals in the infundibulo-pelvic ligament close to one of the ovaries. . . . Wiesel examined fifteen pairs of testicles and epididymes from the newborn and found accessory suprarenal capsules connected with them 23 times: 5 times on each side and

13 times singly. The accessory organs had the same structure that the gland usually shows. They were usually situated in the connective tissue about the vas deferens, and were surrounded by a mass of blood vessels. In older children or adults no fully developed accessory glands were found, but there were remnants in the form of strings and clumps of cells. Aichel, on the other hand, emphasizes the importance of organs found by Marchand near the testes in man and in the broad ligaments of woman, which organs are homologous to the suprarenal bodies."

Stewart also contends that if hypoadrenia means a diminished output of epinephrin, "there is not an experimental fact which shows that this would produce any symptoms at all." He bases this conclusion on the fact that his sections of the splanchnic, bilateral adrenal extirpation, etc., in normal animals did not at once bring on hypoadrenia; because they did not and certain animals did not show its symptoms after weeks and even months, hypoadrenia now recognized by thousands of physicians, does not, he concludes, exist—at least as the supposed expression of a diminished epinephrin output.

To establish such a conclusion on a sound basis would necessitate knowing just what double adrenalectomy does in animals and what function this operation inhibits or arrests and thus make it possible to explain the character and meaning of the symptoms it provokes. Judging, however, from various statements in his paper, Stewart is no better off in this respect than was Swale Vincent (5) five years ago when he wrote: "We know nothing of the *functions** of the adrenal body regarded as an organ on its own account."

Such a result after sixty years, the period elapsed since Brown-Séquard began his work upon the physiology of the adrenals, and notwithstanding an enormous amount of labor devoted to these organs by physiologists since, cannot but suggest that they have been all along on misleading paths. Is there not a more promising field of research, one in which their labors would prove more fruitful? That such a field has been available for nearly two decades, among the many postulates vouchsafed, now seems certain, judging from the fact that all the data accumulated during that period, physiological, clinical, biochemical, etc., have tended to demonstrate its soundness. Even Stew-

*The italics are my own.—S.

ard and Rogoff have contributed much confirmatory experimental evidence. The nature of this field will develop as we proceed.

Reviewing some of the physiological work on record and also some of his own, Stewart recalls that while removal of both adrenals in laboratory animals, dogs, cats or guinea pigs, is promptly fatal, there are exceptions. Frogs and rats stand out prominently among these. Hibernating frogs, for instance, have survived as long as 13 days and summer frogs 48 hours, while 50 per cent of the rats lived as long as 5 or 6 months. Although such animals might exhibit a normal temperature, appetite and strength similar to those observed in operations not involving the adrenals, the time came when more or less suddenly there appeared anorexia, marked myasthenia and a hypothermia of as many as 18° F., followed by death. Yet, Stewart believes that there is nothing especially pathognomenic in these symptoms, except perhaps the rapid myasthenia.

What is the underlying cause of the prolonged survival of the animals? As to the rats, Stewart grants that the survival of so many of these animals may have been due to the presence of accessory adrenals. We have seen the frequency of such in various parts of the body even in human beings, but rats are well known to be particularly well supplied with these accessory structures, both cortical and medullary. There is an important feature which Stewart has overlooked, however, in his numerous references to Boinet's work. It is the presence of hematoidin crystals in 75 per cent of his 109 rats deprived experimentally of both adrenals. It was found practically everywhere, including the lungs. Two fatal cases of Addison's disease were also found to present this phenomenon. Why should this product of broken down hemoglobin result from destruction, both experimental and pathological, of the adrenals?

Fifteen years ago (6) a study of bronzing led me to the conclusion that this pigmentation was due to an accumulation of adrenal substance similar at least to melanin in the cutaneous epidermal layer, and that hematoidin found broadcast in the tissues was similar to the cutaneous melanin. We know also that the skin of batrachians, which takes part in their respiration, contains fluids which, on exposure to the air, first become brown then black, precisely as is the case in Addison's disease. The melanophores of the horned toad were found by Redfield (7) to

contain a substance similar to adrenin. Abel (8) also "found adrenin in relatively enormous quantity in the skin glands of the toad." Again, I had also described the adrenal substance forming part at least of both hematoidin and melanin as an oxidase (adrenoxidase). Recently, Bittorf (9) also concluded that the bronzing of Addison's disease was due to the formation of an oxidase in the cutaneous epithelium.

These few facts, only submitted as mere clues to a possible connection between the adrenin and hemoglobin, would, if true, go far towards explaining the prolongation of life and the non-occurrence of hypoadrenia in animals deprived of both adrenals. Thus in the hibernating frogs of Abelous and Langlois to which Stewart refers and in which the post-operative life was 12 to 13 days, the participation of adrenin in the respiratory process and its presence in this animal "in enormous quantity" would supply a residual reserve quite sufficient to explain their prolonged survival, particularly in view of its greatly slowed consumption. Indeed, as observed by Pembrey (10), hibernation even in animals gave as low a respiratory quotient as 0.3-0.4.

Does, however, adrenin actually take part in tissue respiration? There is no doubt that there is ample room for improvement of our conceptions in this very connection, for as Halliburton states in the last edition of his text-book of physiology (11), "our knowledge of tissue respiration is so scanty that we can say little of its pathological bearing."

That adrenin does take part in pulmonary and tissue respiration by becoming a part of the hemoglobin molecule, I have been urging repeatedly during the last twenty years. Having introduced various data on the subject in the presidential address before the 1918 meeting of the Association for the Study of Internal Secretions, and which, therefore, were published in this journal (12), I will submit in the present connection only the complementary data and those strictly necessary to illustrate the present status of the question.

As preamble, it may be stated that the respiratory process has been *sub judice* ever since 1856, when Vulpian, and subsequently Paul Bert, Müller and other physiologists found flaws in the diffusion doctrine. It failed to account for the disappearance of all the oxygen in the air in the lungs of strangulated animals, also to explain oxygen tensions in the arterial blood

exceeding greatly those in the respiratory tract, etc. Briefly, these and other disturbing factors led Bohr (1891), a Danish physiologist, to urge the need of a substance having greater avidity for oxygen than the blood itself in order to explain the respiratory process. Bohr's view was sustained by several of his colleagues, Haldane, Lorrain Smith, Harley and others. They failed, however, to identify the substance needed.

In 1903 (13) I first published the personal conclusion that it was the adrenal secretion which carried on this function, having been led to it mainly by laboratory studies (1) of the respiratory system in lower animals, including insects, crustaceans, mollusks, fishes, batrachians, etc., ascending the phylogenetic scale to man; (2) of the biochemical reaction of fluids connected with the respiratory process; (3) of the anatomical relations of the organs exposed to external oxygen-containing media; (4) clinical observations; and (5) comprehensive studies of the literature bearing upon these subjects. All these finally pointed to the adrenals, particularly in view of the marked reducing properties of their extracts long emphasized by Vulpian, Cybulski, Langlois, Battelli and others, as the only organs capable of fulfilling the conditions specified by Bohr.

The presence of the colloid hyaline granules which constitute the adrenal secretion in the adrenals themselves and also in their efferent veins, which in turn carry the adrenin-laden blood to the inferior vena cava, is so well established that testimony to this effect is unnecessary. But is it contained in the caval blood and does it reach the heart? Its presence in both is shown by the fact that when this blood contains adrenin in deficient quantity the functions of the heart are depressed, while an excess of adrenin in the same blood increases its tone. Thus, when Stewart and Rogoff (14) compressed the adrenal veins, arrhythmia was caused; this ceased, however, when the veins were released, thus restoring the flow of adrenin to the inferior vena cava and the heart. Again, while the same physiologists (15) noted that section of the splanchnic nerves greatly diminished or abolished the discharge of adrenin, van Anrep (16) found that when these nerves were stimulated, the cardiac tone was increased, and that this failed to occur when both adrenals were extirpated. Fühner and Starling (17) observed that while asphyxia caused the heart to dilate, the injection of adrenalin caused contraction of the

heart and raised the blood-pressure in the pulmonary artery. Besides observing that clamping of the adrenal veins caused arrhythmia, Stewart and Rogoff (18) found that when the heart became irregular after sufficient doses of strophanthin injections of adrenalin restored the cardiac rhythm.

The next question in order is whether adrenin is actually present in the lungs. Not only is such the case but it seems to facilitate the free circulation of air in the air-cells by causing dilatation of the bronchioles. M. L. Menten (19), for instance, found adrenalin in the venous blood of the pulmonary capillaries. D. E. Jackson (20) observed that adrenalin caused prompt dilatation of the bronchioles when these are contracted independently of any rise of the blood-pressure. W. R. Dixon (21) obtained a similar action of adrenalin in the decerebrated cat, and noted a simultaneous increase of the volume of air entering the lung.

The crucial test, however, is whether adrenin when added to it can actually change venous blood into arterial blood on exposure to the air by causing its hemoglobin to be converted into oxyhemoglobin. Even this feature of the process has proven true. While Kariya and Tanaka (22) found that adrenalin could itself act as does hemoglobin, Menten and Crile (23) observed that blood from the adrenal vein invariably assumed a bright red arterial color in from one to twenty minutes after dilution with salt solution, while blood from other organs treated in the same manner showed no change. Battelli (24), Kraus (25) and others have found adrenalin in the blood, while Mulon (26) found that the red corpuscles also gave the histochemical reactions of adrenalin. Menten (27) also noted that adrenalin added to human venous blood caused an increase in the oxyhemoglobin absorption bands.

Moreover, adrenin gives rise to all the physical phenomena of the respiratory process. It increases the intake of oxygen, the output of carbon dioxide, the volume of air breathed, the respiratory excursions of the lungs, the depth and rate of respiration. Thus, it was found to increase the intake of oxygen and the output of carbon dioxide by Byelaventz (28), while Bernstein and Falta (29) noted that 1 milligram of adrenalin sufficed to do so, and Menten (30) observed that it "does particularly affect the oxygen exchange" in the lung. Tompkins,

Sturgis and Wearn (31) found that intramuscular injections of adrenalin caused an increase both in the total gaseous metabolism and the volume of air breathed. Sandiford (32) specifies that all these phenomena were produced in her experiments irrespective of any action on the blood-pressure. The respiratory excursions of the lungs were found by Januscke and Pollak (33) to be increased by doses as small as 1/600 grain (0.0001 Gm.) of adrenalin, while Nice, Rock and Courtright (34) observed that adrenalin increased the depth of respiration whether it raised or lowered the blood-pressure.

Another crucial question is whether adrenin is secreted in sufficient quantity to meet the needs of pulmonary and tissue respiration, i. e., metabolism, in which it necessarily takes part. I attach importance to this factor because it was at one time justly suggested as an obstacle by a physiological friend, whose opinion was based upon the figures of Trendelenburg and Battelli, since shown to be erroneous. Biedl and also Stewart and Rogoff (35) obtained very different results. The latter physiologists state that "the amount of epinephrin spontaneously liberated in cats was found to vary in different experiments within a rather narrow range considering the differences in the conditions, from 0.0008 to 0.0028 mgm. per minute per animal, or from 0.0003 to 0.001 mgm. per minute per kilo of animal." At this rate taking the minimum figure as basis, a man of 65 kilos would receive 2.70 mgm. in his blood in twenty-four hours. This is ample to meet the needs of systemic oxidation, particularly in view (1), of Schäfer's observation that fourteen millionths of a gram of the adrenal principle per kilo of animal sufficed to produce maximal effects, and (2), of the fact that the adrenin secreted probably serves only to replace that which is lost or destroyed, many examples of which I have submitted in various writings.

Finally, that adrenin takes part in tissue oxidation, i. e., metabolism, is shown by its influence on the temperature, basal metabolism and urea excretion, while the converse occurs sooner or later, as every one knows, after removal of both adrenals. The evidence to this effect includes such an array of facts contributed by internal medicine, pathology, pharmacology, comparative anatomy, etc., that a mere fraction of this testimony can be submitted here. Briefly, Oliver and Schäfer (36), Morel

(37), Lépine (38) found that adrenin caused a rise of temperature; Reichert (39) observed that this was accompanied by accelerated metabolism. Large adrenal grafts cause a rise of temperature so great as sometimes to cause death, as observed by Courmont (40), Bra (41), and Jaboulay (42). Malignant adrenal tumors, regardless of histological structure, were also found by Israel (43) to run a febrile course independent of any fever-producing complications. Sandiford (44) found that 0.5 c.c. of adrenalin always caused in endocrine sufferers (73 experiments) an increase in the basal metabolism rate. Tompkins, Sturgis and Wearn (45) observed that the rise in respiratory quotient preceded the acceleration of metabolism. Addis, Barnett and Shevky (46) found that adrenalin in not too large or too small doses in rabbits increased the excretion of urea.

Conversely, I may recall that Brown-Séquard and many physiologists since his time, have noted a decline of temperature in animals deprived of their adrenals, a leading symptom also of Addison's disease along with every sign of slowing of the metabolic rate. The basal metabolism of adrenalectomized cats, carefully controlled by Aub, Forman and Bright (47), showed a reduction of 25 per cent, while the same operation in rabbits was found by Bevier and Shevky (48) to cause a depression of the excretion of urea.

I might add that while German reviewers originally, that is to say in 1903 (49) characterized this function as the outstanding feature of my labors on the adrenals, Weil in his recent (1921) book on the endocrines (50), concludes that the suprarenal gland is directly concerned with oxidation.

If facts count at all, the data submitted should suggest that I was not on the wrong path when I wrote in 1903 (51): "1. The adrenals secrete a chromogen—a colloid, hyaline fluid—which leaves the organs through the suprarenal veins, and is mixed with the plasma of the venous blood in the inferior vena cava. 2. When the venous blood reaches the pulmonary alveoli the marked affinity of the adrenalized plasma for oxygen causes it to absorb this gas from the alveolar air. 3. The carbon dioxide in the blood is thus forcibly replaced by oxygen and expelled with corresponding vigor. 4. The red corpuscles, after this operation, bathe in an oxygen-laden medium, and their hemoglobin becomes reconverted into oxyhemoglobin."

The purpose of this evidence being only to point out the vast reserve which a normal animal may possess, I will not introduce the data which point to the role of the red corpuscles in the process—one quite different from that now taught, nor the special role in it of the adrenal medulla. Neither will I review what knowledge we possess of the connection of the cortical portion of the adrenals therewith.

Briefly, in the face of all the above evidence, Stewart's condemnation of hypoadrenia as this syndrome is interpreted by clinicians does not appear justified. His argument based on the survival of experimental animals after removal of both adrenals and the absence of symptoms during that period are invalidated if, in addition to the *numerous accessory or aberrant adrenal tissues in the body,* there exists a *large systemic supply or reserve of adrenin* from which a normal animal deprived of both adrenals can draw for a time, i. e., as long as its reserve will last, then show the symptoms of adrenal failure and die. The presence of such a reserve has been indicated by the *widespread distribution of hematoidin and of melanin, both hemoglobin bodies of which adrenin forms part,* after removal of both adrenals in rats and in advanced Addison's disease, and the *connection of adrenin with hemoglobin in the respiratory process.*

The suddenly produced morbid process which double removal of the adrenals entails differs entirely, we have seen, from that recognized as hypoadrenia by clinicians. For them hypoadrenia means a gradual failure of the adrenals, which renders these organs unable to supply the body at large the stock of adrenin it needs to carry on, from my viewpoint, its respiratory functions, i. e., tissue oxidation. Whether due to local lesions, or to conditions such as an acute febrile process, which drain the reserve beyond the restitutive efficiency of the adrenals, the result is the same: there comes a time when in addition to symptom complex of the causative disease, there appear certain specific symptoms which are those of gradual adrenal failure. Now what are these symptoms? They are precisely those observed in animals deprived of both adrenals, when the function I have attributed to the latter, tissue oxidation, is taken into account, to-wit: anorexia, muscular weakness progressing to paralysis, loss of tension of the eyeballs, gradual fall of the

blood-pressure and steady fall of the temperature until death ensues.

It would take too much space to adduce all the evidence available, but what I have submitted should suffice to indicate that physicians who have observed and described hypoadrenia in its various forms were justified in doing so. Referring only to adrenopathies, Pende had good ground for his acceptance "of the hypoadrenal constitution as a clinical and pathological entity." The group of cardiopathies of the hypoadrenal type observed in soldiers described by Satre is also a defensible entity, a statement which applies as well to the sudden deaths from adrenal asystole described by Josué. The syndrome of hypoadrenia observed in soldiers suffering from infectious icterus, dysentery, typhoid, excessive fatigue, etc., is equally justified. I have myself observed and studied the majority of these pathological states, and there is no doubt that with the adrenals interpreted as participants in pulmonary and tissue respiration, appropriate replacement organotherapy, adrenalin mainly (using the suprarenal gland in chronic conditions such as Addison's disease), is a life-saving measure often so marked as to suggest undoubted resuscitation.

It was I, moreover, who called attention in 1903 to the fact that Asiatic cholera was "in reality the gravest form of adrenal insufficiency" with "marked muscular weakness," "pulse rapid and weak, sometimes intermittent," "temperature in mouth and surface very low," "respiration frequent and difficult and cyanosis"—all typical signs of adrenal failure similar to those observed when after the period of survival after removal of both adrenals an animal approaches the moribund state. The endotoxins of the cholera vibrio were since found by Déméstrescu (52) to cause disappearance of chromaphil reaction of the adrenals. Confirming my views, Drake-Brockmann 1910), Plovesana (1912), Naamé (1914) used adrenalin and noted a remarkable tolerance, while its efficiency was striking.

Stewart might urge in this connection that "there is nothing specially pathognomonic in such symptoms unless indeed it be the muscular weakness which may seem to come on with more rapidity, etc." Yet, the fact that he cannot himself explain their origin with all experimental data at his disposal is suggestive. Nor can anybody, in my opinion, do so *without*

taking the role of adrenin in tissue oxidation into account. It is the key to the whole situation and with scientific accuracy explains the syndromes of both the adrenal insufficiency due to complete destruction of the adrenals, as it is interpreted by Sergent, and hypoadrenia as it is interpreted by myself, a larval form devoid of permanent invalidating lesions, which may be produced by many pathogenic conditions, and the non-recognition of which would be a calamity to a large proportion of the sufferers entrusted to our care.

Stewart refers to "exact physiological science" as the basis of his criticisms of clinicians' conclusions. The foregoing analysis indicates, if I am not mistaken, that while of incalculable value in its own legitimate field, physiology does not convey the truth when it undertakes alone to analyze pathological phenomena. When a pathological state is produced in a normal animal by physiological methods, *it portrays only what the same methods would provoke in man;* and even then allowances would have to be made. As a standard for pathological states which necessarily introduce many fundamental deviations from the normal, however, experimental physiology in *normal* animals tends to mislead. Indeed, as in the case of suprarenal insufficiency or hypoadrenia, it may prove costly in human lives—a fact which should inspire great reserve in the presence of therapeutic results attained, even though they disagree with experimental observations which at best, judging from the fate of the theories of Oliver and Schäfer, Abelous and Langlois, Cannon and other physiologists of the first order, cannot but offer a frail foundation for a final judgment. Meltzer has wisely condemned experimental control over measures found useful.

An experience of over forty years as a physiologist (my first chair), clinician, encyclopedist and editor, has only served to emphasize the fact that physiology will become a "great white light" when physiologists will fully realize that its true worth lies in *constructive synthesis* along with contributions from all other branches of medical science. Hence the fact that even the comparatively few data submitted in the foregoing pages in support of the respiratory doctrine, include contributions from several subdivisions of medical knowledge, clinical medicine, physiology, pathology, pharmacology, biological chemistry, zoology, etc. These are not used in the manner sometimes ob-

served in comprehensive works, where each branch is tersely reviewed separately, but they are made, instead, to participate in the upbuilding of each subdivision of the subject studied, thus forming in the end (the conclusion or postulate reached) a mosaic, as it were, of all knowledge available on the subject. Apparently discordant data, always considered with due respect, often prove not to be such, for, if based on sound observation, they usually find in the other branches of knowledge one or more links which convert them into valuable assets. As examples, I might mention the "obsolete" tonus theory of Oliver and Schäfer, the "obsolete" antitoxic theory of Abelous and Langlois, and the much questioned emergency theory of Cannon, which though severely assailed by physiologists, are to me brilliant and invulnerable contributions to our knowledge when regarded as manifestations of the function I have attributed to the adrenals, and when they are elucidated by the many sidelights it affords.

It is because I have followed this plan, which does justice to all sincere workers, that my interpretations of the main endocrines, even though seemingly anomalous at first, have, as we have seen in the case of the adrenals, been sustained by experimental and clinical evidence from all directions. No one today would dare to state that we have reached beyond the threshold of endocrinological knowledge; but it is essential for the welfare of suffering mankind, the clinician's main concern, that even the threshold be that of the right door.

In closing, I cannot but emphasize anew what I have long urged. This is that the *harmonious cooperation of all medical scientists*, each branch being regarded as a spoke in the wheel of progress, will in the end prove to be the best policy. In no field of human endeavor is this attitude more needed today than in endocrinology.

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THE INFLUENCE OF THE ENDOCRINE SYSTEM ON INTRAOCULAR TENSION

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This report comprises a short summary of my clinical observations as regards the relation between intraocular tension and the internal secretions. The way such a relationship was suggested has been already published (1, 2). This report is presented in the hope that it will lead others to extend the observations in cases of different dysfunctions of the various endocrine glands.

The current theories which seek to explain the regulation of intraocular tension are more or less inadequate to account for our clinical experiences. Even those based on blood pressure are unsatisfactory, because we find that: (1) the tension of normal eyes can change without change of the blood pressure; (2) there are cases in which the eyes of young individuals with relatively high blood pressure show a lasting hypotension; (3) we find sometimes in case of normal eyes a remarkably high tension, although the blood pressure is normal or even lower than the average for the given age.

These facts interested me particularly because I have made systematic studies with the tonometer of Schiötz since 1910 (3) and was led to the conclusion that the long discussed problem of glaucoma will not be solved either by anatomical studies alone or by studies of the blood pressure and changes in the intraocular blood vessels. We have reason to believe that acute inflammatory glaucoma as well as so-called simple glaucoma is only a manifestation of certain constitutional abnormalities. I should like to go a step further and say that even those anatomical anomalies predisposing to glaucoma could be looked upon as probable consequences of certain constitutional anomalies. This conclusion is suggested by knowledge of certain families, several members of which have an unusually great degree of hypermetropia, small eyeballs with relatively large lenses, etc.

Three years ago quite an unusual case was observed in my eye clinic in Pozsony, Pressburg,* which afforded a hint to go farther in studies along this line. The patient was a pregnant woman who showed signs of osteomalacia. Her eyeballs lost their original form, the cornea of both eyes was wrinkled and the eyeballs were so soft that the simple cohesion between the conjunctiva tarsi and bulbi was enough to lead to a deep wrinkle on the upper part of the sclera when the lower lid was pulled down.

The normal intraocular tension is between 15 and 26 mm. Hg pressure and when the heart stops beating it sinks to 8 mm. Hg. In this case the intraocular tension was less than that of a cadaver, it being even less than 5 mm. Hg. I searched for the explanation and what first set me to thinking was a coincidence of pregnancy and osteomalacia. I reflected that either of these conditions may lead to some degree of subtension and the two together all the more.

This conception led to a systematic examination of the eye tension of pregnant women. We found that among 50 subjects there were 42 with decidedly subnormal tension, two with normal and six with high tension. Those who had hypotension of the eyes showed the signs of pregnancy in the face, hands, skin, etc. These signs are regarded as due principally to hyperpituitarism, which is more or less pronounced in case of pregnancy (Erdheim and Stumme). The average tension of the 42 pregnant women was 12 mm. Hg, i. e., much less than the average normal eye tension, which is 20 mm. Hg.

Those who had hypertension—and one had even 31 mm. Hg pressure, although the eyes were clinically normal—looked unusually fresh in spite of their pregnancy and the facial signs of pregnancy in the lines and color were totally absent. It may be supposed that in these cases the ordinary hyperfunction of the hypophysis was not present.

In the meantime, we had opportunity to examine a patient who had atrophy of the optic nerves, bitemporal hemianopsia, cessation of menstruation and enlarged sella turcica, as shown by radioscopy. The intraocular tension in this case was 11 mm. Hg

*The Elisabeth State University originally was located there; in the summer of 1919 the Chech government compelled us to leave it. Since then the work is carried on in Budapest.

in the right eye and 12 mm. in the left. A second and a third case of hypophysis tumor showed similar hypotension.

One patient showed typical signs of acromegaly, but for a considerable time had been under x-ray treatment and for several months had received thyroid tablets; the pathological process had been arrested as shown by the fact that for two years the measurements of the bones, extremities, etc., had not changed. In this case visual acuity as well as the field of vision was the same as two years before; the tension was perfectly normal. This spoke for the fact that the balance of the endocrine system had been restored. This observation offers hope that we shall be able to use these ocular tension examinations to decide whether in certain cases treatment has had a satisfactory effect.

This supposition seems to be strengthened by a few cases of osteomalacia. Two cases which were not treated before the examination of the tension took place, had very decidedly low eye tension (the one 12 and 13 mm. Hg, the other less than 5 mm.). Of the three patients which were operated upon (castration) before we examined their tension, one failed to show any conspicuous improvement of the clinical symptoms; she could not stand on her feet and had as much pain as before the operation. This patient had subtension (12 mm.) in both eyes. The other two, who got decidedly better, had normal tension. The only remarkable circumstance was the great difference of the tension between the right and left eyes. The rule is that both normal eyes in any given subject have the same tension. The tension in one of these cases was 23 mm. Hg in the right and 15 mm. in the left eye; in the other case it was 18 mm. in the right and 15 mm. in the left eye.

The only previous publication which gave a hint that abnormal eye tension may be connected with dysfunction of certain endocrine glands was that of Hippel (4), who found that patients with glaucoma gave a positive Abderhalden reaction with thyroid and thymus. Although these findings did not induce many investigators to extend the studies, they deserve the greatest attention.

Later on, Hertel (5) found that patients with hyperfunction of the thyroid have low intraocular tension and patients with glaucoma have signs of hypofunction of the thyroid. Wessely

(6) affirmed that the eye tension of patients with Graves' disease is in most cases lower than normal.

My experience does not confirm this. I have found among patients with Graves' disease more who had high tension than low tension; several with decidedly low tension were seen, however. In the older literature we find several articles with the statement that in Graves' disease the high tension of the eye is not a rare exception. Brailey and Eyre (7) several times found deep excavation and high intraocular tension in such cases. They, however, did not use a tonometer, but judged by touch only. Gail (8), too, in one case of Graves' disease, found high tension and deep excavation of the optic nerve. In Hippel's article we find a case of Graves' disease ("forme fruste") connected with glaucoma simplex.

It would seem unsafe, therefore, to accept as generally true the statement regarding the low tension in Graves' disease. This apparent contradiction in the results of our examinations is easy to understand if we consider the great variability of the symptoms of this illness. In my experience Graves' disease can cause either type of abnormal eye tension. But in either case we find almost regularly a remarkable difference of tension between the right and the left eyes, and a pronounced *lability* of the tension even during the measurement. This proves that the regulation of the tension is disturbed.

SUMMARY

We find that a disturbance in the balance of the endocrine system causes a disturbance in the intraocular tension. When the balance is restored the intraocular tension approaches or becomes normal. Therefore we may conclude that the hitherto unsettled question of the regulation of the intraocular tension depends primarily on the function of the endocrine glands. Although the disturbed function of one gland of this system provokes a change in the function of others and, therefore, we usually have to do with a pluriglandular disturbance, the glands that seem to play the principal role in the regulation are the hypophysis, thyroid, thymus and gonads.

Determining of the lasting changes in the intraocular tension may give us important hints and may be used as a valuable diagnostic help when we suspect some disturbance of the endo-

crine system or in the function of one certain gland. We recommend, therefore, the careful and systematic measuring of the eye tension with the tonometer as a diagnostic and in some cases prognostic auxiliary method.

Further observations and therapeutic findings, which are purely of ophthalmological interest, will be published in special ophthalmological journals.

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A CASE OF RETARDED MENTALITY IN A CHILD, TREATED BY ORGANOTHERAPY

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Inasmuch as endocrinology is relatively a new branch of medicine, and the knowledge of the ductless glands and of the influence they exert upon the living organism is yet in its infancy, it is the view of the writer that clinical data are at least as valuable as data obtained in laboratories from observations upon animals. This may serve as justification for publishing the following case.

This is the case of A. F., a girl of 14, of healthy parents and whose birth was normal. When a year old she had convulsions, that came on an average of twice a year until she reached the age of six. Then the convulsions ceased. Measles and tonsilitis were the only diseases the child had gone through. Though her physical development up to about two years ago was apparently normal, her mental development caused her parents considerable anxiety. It took her eight years to complete the first five grades of school, she being obliged to remain two years in each of the last three grades. A tonsillectomy and adenectomy was performed with the view of raising her intellect, but without any perceptible effect on the patient. Her growth during the last two years was suddenly very rapid, and she became tall and lank, but her mental capacities either remained stationary or developed very slowly. She lacked concentration — she often returned her library books without reading them. Broken dishes and faulty chores were frequently the despair of her parents.

With such a history this girl came under my observation on Sept. 27, 1920. The following data were obtained: The girl was tall for her age and weight, measuring 62 inches in height and weighing 86.5 pounds. She had long arms, large hands, long fingers, long legs and large feet. Otherwise physical examination was negative. Her mentality corresponded approximately to that of ten years. At the time of my first examination the patient was in the fifth grade, this being

her second year in the same grade. The patient was given capsules three times a day, containing the following formula:

Pituitary Gland (anterior lobe)	gr. ii
Thymus gland	gr. i
Thyroid gland	gr. 1/12
Calcium Phosphor. Comp. q. s. ad	gr. v

With the exception of two months, March and April, 1921, the patient was taking these capsules regularly from October, 1920, to July, 1921. In March and April she ceased to take them because her brothers teased her, implying that her "wisdom" and smartness came from these capsules.

5. (1914) Last Name Y — First Name and Initial A. O

BOSTON PUBLIC SCHOOLS
PUPIL'S REPORT CARD

Grade 2 — Room 14

1 = Excellent
2 = Good
3 = Fair or Passable
4 = Unsatisfactory
5 = Very Poor

SCHOOL YEAR 191 · 191	Number of Sessions Absent	Number of Times Tardy	Conduct	Effort	Reading and Literature	English	Spelling	Penmanship	Grammar	Arithmetic	Geography	History and Civics	Music	Drawing	Manual Training or Domestic Arts	Physiology and Hygiene	Science	Physical Training	EXAMINED BY
	Ab.	T.	C.	Eff.	R.&L.	E.	Sp.	Pe.	Gr.	Ar.	Ge.	H. & C.	M.	D.	M. or D.	P. & H.	Sc.	P. T.	
Sept. & Oct.			3	2	3	3	2	2		2	3		1	2	3			1	
Nov. & Dec.			1	1	3	2	2	2		2	1		1	2	3	2		1	
Jan. & Feb.			1	1	2	2	1	2		2	3		1	2		1		1	
Mar. & Apr.			3	3	2	2	1	3		4	4		1	3		1		2	D.F.G.
May & June			1	1	3	3	1	3		3	3		1	3		1		1	

"THE HOME AND THE SCHOOL SHOULD WORK TOGETHER FOR THE GOOD OF THE CHILD."
It is important that the teacher should be fully informed as to the child's physical condition, life outside of school, and previous history. Parents are cordially invited to confer with the teacher or the principal.

School: Garrison — Signature of Teacher: Marguerite Rich

Library Bureau U67890

With this in view, it is interesting to study the reproduction of the original school card, where her school work was marked bi-monthly. It is seen from this card that her November and December record was a great improvement over the one of September and October, while the January and February record shows a still further advancement. The March and April record is quite in accord with the omission of the capsules during these months, while the resumption of these capsules during the months of May and June resulted again in a considerably improved school record.

On Feb. 11, 1921, her height was 63.5 in.; her weight was 92 lbs.; her span (from middle finger to middle finger), 63.5 in.; her pulse, 80; blood pressure, 60-100; secondary sex characteristics (enlargement of the breasts, growth of pubic and axillary hair) present.

On Nov. 6, 1921, the following data were obtained: Height, 64 in.; weight, 98½ lbs.; span, 64 in.; blood pressure, 50-110; pulse, 80. Her first and only menstruation occurred two months ago.

COMMENT

The history of the case—convulsions during the first six years, the sudden growth in the last two years, the present stature, the span being equal to or even exceeding the height, the backwardness—all this points to a so-called mild form of gigantism, a condition that is supposed to result in growing children from an abnormal activity of the anterior lobe of the pituitary gland. It is the same process that brings about the characteristic symptoms of acromegaly in adults. The supposed abnormality of the anterior lobe called in my formula for two grains of anterior lobe pituitary, the small dose of thyroid being added on the principle that the latter is a strong synergist with the former; the thymus gland was also added because of its supposed influence upon the skeletal growth of the child, and finally the salts were added as a hematic.

The writer is fully aware of the warning given by Cushing (1), Hoskins (2), and others, of the danger of overestimating the efficacy of organotherapy. Granting the timeliness of this warning, we must not go too far in the opposite direction and underestimate the importance of clinical observations carefully and conscientiously made. We must not forget that, after all, the experimental observations in the laboratories must be first translated into clinical observations before their full significance and importance is made clear.

SUMMARY

The case is described of a girl 14 years of age who had manifested rapidity of growth and developed skeletal proportions suggestive of gigantism. Considerable mental retardation was evidenced. Obvious improvement in her scholastic record was seen while she was undergoing organotherapeutic treatment. Renewed retardation occurred when treatment was discontinued and there was improvement with its resumption.

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STUDIES OF THE THYROID APPARATUS. V. THE SIGNIFICANCE OF THE COMPARATIVE MORTALITY RATES OF PARATHYROIDECTOMIZED WILD NORWAY RATS AND EXCITABLE AND NON-EXCITABLE ALBINO RATS

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In the first paper of this series (1) a report was made of a comparative study of the mortality rate of two groups of parathyroidectomized albino rats. Although the members of both groups were descendants of the same parent stock they differed in the general trend of their excitability or readiness to respond to exogenous stimuli and consequently in their muscle tone. The one group, called the "Stock Albinos," presented the normal picture of low threshold of response to stimulation and high muscle tone. These rats were easily excited. The mortality rate within 48 hours after parathyroidectomy was 79 per cent and was accompanied by *tetania parathyreopriva*. In the other group, designated as the "Gentled Albinos," in which excitability and muscle tone had been reduced to a low level by constant handling and petting, the mortality rate was but 13 per cent.

As a result of these observations the hypothesis was advanced that the occurrence or non-occurrence of early death from the loss of the parathyroid glands depended in large part on the general trend of the reactions of the organism to exogenous stimuli. These reactions were considered as being mediated by the relative degree of control of the animal by the instincts of flight and pugnacity as manifested in their affective aspects of fear and anger. In these reactions the nervous system is obviously the directive mechanism. Consequently the stability of the nervous system was considered as a factor of importance in the resistance of the albino rat to the loss of the parathyroid secretion.

On the basis of this hypothesis it seemed desirable to determine the mortality rate of the untamed wild Norway rat caged

for one or two generations. This animal gives the impression of a very excitable organism in which the instinct of pugnacity is apparently more highly developed than in the "Stock Albinos."

The Norways used in this series were kindly furnished by Doctor Helen D. King from her stock and were of the F_2 generation. Rats of both sexes and of different ages were used. The sex and age distribution approximated that of the earlier study. The conditions of diet and caging were likewise the same. Inasmuch as this investigation was confined to the determination of the mortality rate due to the loss of the parathyroid secretion, and since it had been previously found that identical mortality rates obtained whether parathyroidectomy or thyro-parathyroidectomy was done, the latter operation was done on the majority of rats at this time for purposes of convenience. As in the first study, 48 hours from the time of operation was taken as the standard of survival.

A total of 102 rats was used. Of this number 92 died within the stated period. All of the rats save three showed tetany. The mortality rate of the wild Norway rat due to the loss of the parathyroids is thus 90 per cent. This rate is higher than that for the excitable "Stock Albinos," a result which was to be expected and supports the original hypothesis. A comparison of the mortality rates of the three groups is given in the accompanying chart.

The difference between the two excitable groups is actually greater than the relative values indicate because of the fact that most of the survivors of the 48 hour period of the Norways died within two or three weeks after the operation, while most of the survivors of the "Stock Albino" group lived until killed for other purposes (for two or three months).

The interpretation of these differences on the basis of the stability of the nervous system is further supported by the fact that when a litter of eight pure black rats 75 days old, which are normally as excitable as the wild Norway, was parathyroidectomized all but two survived the 48 hour period. These rats had been tamed to the point where they gave but little evidence of fear or anger and where the muscle tension on handling was

obviously of a low order. All other conditions such as diet and caging were the same as for the other groups.

On the basis of these results it is possible to explain the differences in the observations of other investigators on the survival or non-survival of the rat from the loss of the parathyroid secretion. Cristiani (2), Erdheim (3) and Iselin (4) found a high mortality rate after this operation. Vincent and Jolly (5), Farner and Klinger (6) and others report the contrary. The

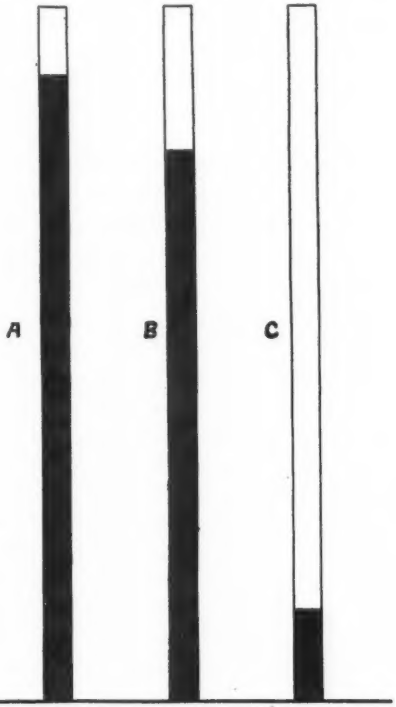


Diagram showing relative mortality after parathyroid extirpation in wild Norway (A); untamed Albino (B); and gentle Albino rats (C).

latter also failed to obtain tetany after parathyroidectomy of five adult wild Norway rats caught in the open and of unknown age. On the other hand, I removed the parathyroids from three Norways over two years old. They all showed tetany and two

died within 24 hours. Farner and Klinger attribute the low mortality following parathyroidectomy in their rats as compared with the high values found by other observers to differences in the strains used. While this may be a factor, I believe that the differences are due to differences in the intensity of the neural reactions of the various groups in the response to external stimuli as largely directed by the degree of control of the organism by the instincts of flight and pugnacity. That the emotional trend of the individual is an important factor in the degree of resistance to disturbing conditions is well shown from the clinical experiences of Crile (7). This investigator believes that the preliminary stabilization of the patient with the view to removing fear of operation and the consequent lessening of neural tension is an important prerequisite to surgical success. His results are a strong support for this belief. It cannot be doubted that not only does the bodily constitution affect the functioning of the nervous system, but also that the neural activities have a profound effect upon bodily constitution. This I have discussed in some detail elsewhere (8).

The objection may be raised that those rats which survive the extirpation of the parathyroids do so because all the parathyroid tissue has not been removed,—that is to say that in the survivors either accessory or aberrant parathyroid tissue is present. Erdheim (3) and Farner and Klinger (6) have made serial sections of the neck and thymus of rats and report the finding of minute groups of cells simulating parathyroid tissue. Nevertheless they state and apparently believe that this so-called parathyroid tissue can have no important physiological function. Thompson (9) from a similar study comes to the conclusion that the rat has but two functioning parathyroids. It is nevertheless true that there may be occasionally an animal in which a parathyroid may be found aberrant. Farner and Klinger report some 12 per cent of this type. From their brief description, however, it is evident that by far the greater number of these aberrant parathyroids are easily recognizable. I, too, have occasionally found a parathyroid lying adjacent to the thyroid instead of embedded in this tissue as is usual. The percentage of undetectable aberrant parathyroids is very small and can play no significant role in the causation of the wide dif-

ferences observed in the mortality rates of excitable and gentled rats. Moreover, those rats which survive the parathyroidectomy may still show tetany, and disturbances of growth of the incisors occur with remarkable uniformity. Although it is impossible to say definitely that there is no functioning parathyroid tissue in those rats which have survived the removal of the parathyroids from their usual location, yet since only those rats were included in this study from which two well recognized parathyroids were taken, and in view of the facts presented above, the conclusion is justified that the differences between the three groups studied are valid evidence of differences in the respective resistances to the loss of the parathyroid secretion.

This idea serves as a working hypothesis as the following discussion will show.

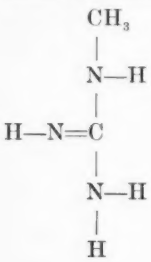
There are at present three theories as to the cause of the tetany occurring in animals following parathyroidectomy. There is the theory of a calcium deficiency in the blood which was developed by MacCallum and Voegtlin (10). This calcium deficiency results in a disturbance of the ion equilibrium of the blood and a resultant increase in nerve irritability. There is the theory advanced by Wilson, Sterns and Janney (11) in which the tetany is considered as a sequence of a disturbance of the acid-base equilibrium of the blood. The observations in support of this idea are as yet too few and too incomplete to justify its acceptance. Moreover, neither Hastings and Murray (12) nor Underhill and Nellans (13) by modern methods have been able to support the observations of the proponents of this theory, while Greenwald (14) presents evidence that the increase in the sodium ion is a contributing factor rather than the so-called alkalosis. Finally there is the theory of Paton and Findlay (15) that the tetany is a result of a toxemia due to the presence of a guanidine compound resulting from protein catabolism.

The observations reported in this and previous papers (1) (16) fit in with this last theory.

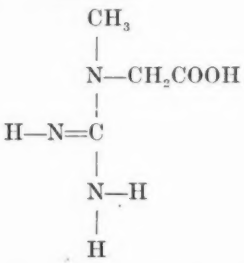
If we assume that a function of the parathyroids is to provide a means to the organism of facilitating the disposal in some way or other of the toxic compound guanidine or methyl-guanidine there is a considerable body of data in support of our hypothesis. For Koch (17) has found that methyl-guanidine

is excreted in parathyroid tetany. This has been confirmed by Burns and Sharpe (18), who also found that methyl-guanidine occurred in increased amounts in the blood of animals in this condition. Recently Nattrass and Sharpe (19) have found that in adolescent tetany there is a marked guanidine excretion. The objection has been raised that the method of determination of methyl-guanidine would tend to change creatine present into that compound in view of the alkalinity of the solutions used. I have found no evidence whatsoever of any decrease in the total creatinine of muscle extracts when incubated for 24 hours at body temperature in alkaline solution (20). Paton and his co-workers and others have found that methyl-guanidine increases nerve irritability. Methyl-guanidine is de-acetylated creatine as the formulas show:

Methyl-guanidine



Creatine



Pekelharing and Van Hoogenhuyze (21) have pointed out the relation between muscle tone and creatine and their general conclusions are supported by the studies of Leathes and Orr (22) and Hammett (23). It appears as if the degree of creatine formation is directly related to the degree of muscle tone. Now if guanidine, or methyl-guanidine, is a normal by-product of that phase of muscle metabolism concerned in muscle tone, then when the parathyroids are removed, and there is removed with them the chief agency for detoxicating the guanidine compound, possibly by assisting in its transformation to creatine as has been suggested by Henderson (24), we should expect to get the evidence of the greater or acute toxemia in those animals in which excitability and its consequent high neural and muscle tension are present, and the lower or chronic toxemia in the gentled

animals where the muscle tone is low because of the high threshold of the nervous system to exogenous stimulation. Such we have seen to be the case.

I would not for one moment be taken as denying the occurrence of a decrease in the blood calcium and a possible disturbance of the ion and acid-base equilibrium, or that these changes may participate in the ultimate outcome. That such disturbances occur in infantile tetany has been demonstrated recently by Tisdell, Kramer and Howland (25), who found that although the calcium concentration of the blood is markedly diminished the amounts of sodium present remain the same. *But these are secondary phenomena.* The relative lapse of time between parathyroidectomy and the appearance of tetany and disturbed acid-base or calcium equilibrium afford no support for the former theories. In fact, it is difficult to believe that the parathyroids are the direct regulators of the sodium-calcium ratio, the ionic equilibrium and the acid base balance of the body. From the available data it is more reasonable to believe that when the parathyroids are removed the organism loses in great part its capacity to get rid of the toxic nerve irritant, guanidine or methyl-guanidine, a product arising largely from the metabolism of the condition known as muscle tone. There is then set up a condition of heightened neural activity. This results, among other things, in a disturbance of muscular activity. As is well known, this leads to marked changes in the respiratory exchange. From this arise changes in the composition of the blood. Thus the ion equilibrium is upset and the various recorded changes occur. That the parathyroids do play some part in the creatine metabolism I have recently shown (16). Their exact role has yet to be determined.

This then is our working hypothesis.

From the observations on the three groups of rats certain general conclusions of practical significance can be drawn. It is evident that the more excitable the organism the higher is the neural and muscular tension, the greater is the instability, the greater is the production of toxic by-products, the greater is the need for the mechanism for getting rid of these poisonous substances and the greater is the dependence of the organism

on the parathyroids in averting disturbances arising from these sources.

The protective function of the parathyroids apparently is of decreasing importance as the tendency for acceptance of environmental changes without protesting response is increased. The result of the diminution of the domination of the emotions of fear and anger, which as Stanley Hall (25) points out is a major impelling motive of man, is a lessening of the production of organic changes which are detrimental to the individual. Resistance is raised. It would appear as if Crile, in his custom of having his patients undergo a preliminary period before operation in which they are familiarized with the procedure of anesthesia and in which by education fear is lessened, has been putting into practical use the principles which these experiments on excitable and gentled albino rats seem to establish.

SUMMARY

The mortality from parathyroid extirpation in wild Norway rats was found to be 92 out of 102 subjects, or 90 per cent. In case of gentle albino rats the mortality had previously been shown to be 13 per cent and of untamed albino rats, 79 per cent. The high mortality is regarded as correlated with heightened neuro-muscular activity and resultant augmented toxin formation. The bearing of these findings on certain clinical observations is discussed.

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THE USE OF PITUITARY EXTRACTS BY MOUTH IN THE TREATMENT OF DIABETES INSIPIDUS

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It has been quite conclusively shown that pituitary extract—posterior lobe—is effective in controlling the polydipsia and polyuria of diabetes insipidus. It has, however, been necessary in practically every case to administer the extract by intramuscular injection. As a rule one injection per day, regardless of the size of the dose, is not sufficient to relieve the patient. Usually two or three injections of 1 cc. each are required to keep down both the day and the night intake and output. Since, in most cases, this treatment has to be continued indefinitely a great financial and physical burden must be endured by the patient. The present price of the liquid extract is about 25 cents per 1 cc. ampoule. Since it usually requires three injections per day the cost to the patient would be $0.75 per day for the extract, alone. To this is to be added the physician's charge for giving the injections, therefore, the cost to the patient could not be less than $1.50 per day. Of still greater importance is the patients' loss in time in being required to make three visits per day at the physician's office.

On looking through the literature we find that in practically every reported case of diabetes insipidus the administration of pituitary extracts by mouth has been tried and reported as a failure. In a few cases the feeding of four to seven whole beef glands has been reported as successfully reducing the polyuria during the night.

In the treatment of the following case it was our purpose to find, if possible, a successful method of giving pituitary extract by mouth. Since there is a strong probability that the effective agent of the extract is destroyed in the stomach, we sought to overcome this possible difficulty by giving the extract in salol coated capsules. The preparation used was the desiccated posterior lobe as prepared by Armour & Co.

The price of the desiccated posterior lobe extract (Armour & Co.) is about $2.00 per dram. This would make the capsules (2 gr.) cost at the rate of fifteen for $1.00. The salol coating would increase this cost slightly. At the rate of four capsules per day the cost to the patient would be $0.35 to $0.50 per day; about one-third the cost of the injections. The great saving to the patient in time and money is quite evident.

CASE HISTORY

Case B.V.—The patient was a white male, age 37, by occupation a railroad brakeman.

His weight at the onset of the present illness was 145 pounds; on admission to the hospital it was 165 pounds; six months after admission to hospital it was 195 pounds.

He was well nourished and well developed, and did not appear to be sick.

He entered Barnes Hospital on March 31, 1921, with the complaint of excessive thirst, frequency of urination, diarrhea and almost constant headache.

His family history was unimportant.

His past history indicated the usual childhood diseases. He had paralysis of right side of face and bilateral impairment of hearing twelve years ago.

Gonorrhea and chancroid, contracted fourteen years ago, received no treatment.

Nine years ago he was troubled with weakness, shortness of breath and nervousness. He lost 30 pounds of weight in one year. He consulted a physician at this time and was told that he had pulmonary tuberculosis and that he could not live over one and one-half years. At this time the patient began excessive indulgence in alcohol. This excessive drinking was continued for several years.

The patient was married nine years ago and has two children living and well. There is a history of one miscarriage.

His present illness began two years ago and the trouble came on quite rapidly. He first noticed that he was drinking large amounts of water and that he had to get up several times at night to urinate.

Within a month after the patient first noticed his increased thirst and frequency he was voiding large quantities of clear urine about every thirty minutes day and night. He states that on several occasions he measured his urinary output for twenty-four hours and found it to be twenty to twenty-five quarts.

From the beginning of his present trouble the patient has had more or less constant headache. He also complains of dizziness and of being easily fatigued. He thinks that his memory is impaired, and states that his head "feels dead."

Since the onset of the trouble he has had four or five loose stools per day. His appetite has always been good.

Since one or two months after the onset, the patient's condition has remained quite constant until he entered Barnes Hospital.

Physical examination gave no definite pathological findings.

Neurological examination showed a seemingly normal mental condition. Judgment and memory were good. There were no speech defects, nor pathological reflexes.

Laboratory and special examination showed normal blood findings. The urine showed a very low (1001-1002) specific gravity on admission; the total solids for twenty-four hours were within normal limits.

The blood Wassermann reaction (four taken) was negative.

One cerebro-spinal fluid Wassermann was taken with negative results.

The phenosulphonphthalin test for kidney function showed a return of 75 per cent of the dye in two hours.

Opthalmoscopic examination showed that the discs were normal.

The visual fields were normal.

Stereoscopic plates of the skull showed no definite abnormalities.

A gastric fractional analysis showed a normal acidity curve.

A gastro-intestinal fluoroscopic examination showed a marked hypermotility of the whole tract.

The blood pressure on admission was 110/65; after treatment it was 125/70.

Progress in the Hospital: When the patient was first admitted to our service his twenty-four hour fluid intake and output ranged between twelve to fifteen liters.

In order that we might secure a more stable intake and output we first had the patient control his intake at a point where he could remain for some time with reasonable comfort. This point was found to be about seven liters per twenty-four hours. After thus limiting the intake for three days the urinary output decreased in proportion and the specific gravity went up to 1011. The patient was now asked still further to reduce his intake. This he did, getting it down, with some difficulty, to slightly less than four liters. The specific gravity went as high as 1013. While on this decreased intake the patient complained of nervousness, dull headache, and sleeplessness.

After keeping the patient on a four liter intake for six days he was put on placebo treatment for four days. The patient thought that this treatment made him less nervous, but it was noted that his intake was gradually increasing.

The patient was now put on 8 minims of adrenalin, t.i.d., by mouth. This failed to control the gradual rise in the intake.

Giving the adrenalin by means of a duodenal tube gave no better results.

The patient was next put on desiccated pituitary extract, posterior lobe (Armour & Co.), in salol coated capsules. The dose was

started at one-half grain, t.i.d., and gradually increased to two grains, t.i.d., a.c. and at 10 P. M. The 10 P. M. dose was found to be necessary to control the nocturia.

On the latter treatment the intake came down to between two and a half and three liters and remained there during the two weeks that the treatment was continued. The patient stated that he felt better than he had since the onset of his trouble. His headaches disappeared, he became less nervous. He had no nocturia. The number of stools decreased from 4 or 5 watery stools per day to one or two formed stools per day. The patient stated that he was quite satisfied with two and a half to three liters of fluid per day. His only complaint was some difficulty in getting to sleep at night. This was relieved by giving eight minims of paraldehyde at bedtime.

Before and during the treatment quantitative tests were made on the urine as follows: for urea, uric acid, creatinine and chlorides. Tests were also run on the blood for non-protein nitrogen, urea, uric acid, and creatinine. These constituents were found to be practically normal in amount. There was practically no variation in them after the urine became more concentrated.

During the treatment with pituitary extract the specific gravity of the urine went as high as 1024 on the night specimen and 1019 for the day specimen.

We next tried the effect of intra-muscular injections of pituitary liquid. Single daily injections of 1 c.c. would reduce the output for about twelve hours; but during the next twelve hours there was a marked polyuria so that the total twenty-four hour output was not decreased. Two injections of 1 c.c. each were effective in keeping down the daily output, provided the second injection was given at about ten o'clock at night. Even with two daily injections the intake and output were not reduced below two and one-half liters. This is no greater reduction than was obtained with the dry extract given in salol coated capsules by mouth.

Whenever the patient was taken off all treatment his fluid intake and output increased in two or three days to seven liters or more.

We now tried giving the pituitary extract powder to see whether it would be as effective as when given in salol coated capsules. The powdered extract was given in a small amount of milk in two grain doses, t.i.d., a.c. and at 10 P.M. This method of treatment proved to be quite ineffective in controlling the polydipsia and polyuria. Giving the powdered extract per rectum in four grain doses twice per day gave no results. The patient was discharged from the hospital on June 15, 1921. At this time he was still keeping his intake and output under three liters.

Since leaving the hospital the patient has been unable to secure a sufficient amount of the desiccated extract and he has passed as much as twenty liters of urine per day.

He also complains of marked fatigue on slight exertion and since leaving the hospital he has been unable to do more than four hours work per day. The fatigue is followed by uncontrollable thirst. The patient feels sure, however, that if he could avoid exertion and could have the pituitary extract regularly, he could control his thirst at any time.

DISCUSSION

It is possible, in this case, that the marked hypermotility of the alimentary tract may so increase water absorption as to cause the excessive thirst, and incidentally the excessive urinary output. It is also possible that the pituitary extract may decrease the absorption of water either by limiting the intestinal motility or by increasing a local vaso-constriction.

The results obtained in this case would suggest that, in some instances at least, diabetes insipidus may be successfully treated by giving the desiccated posterior lobe substance of the pituitary gland by mouth, provided that it is given in such a way as to pass through the stomach unchanged.

Giving the extract in salol coated capsules seems to give a satisfactory solution to this problem.

SUMMARY

The possibility of finding a satisfactory method of administering post-pituitary extract by mouth was investigated. Reduced expense and increased convenience for the patient were the principle factors considered. The history, physical and laboratory findings in a case of diabetes insipidus are given. The progress of the patient under various types of treatment is recorded. It was found that by giving desiccated posterior lobe substance in salol-coated capsules the polydipsia an dpolyuria were as effectively controlled as with hypodermic injections of pituitary extract.

CHILDHOOD MYXEDEMA OR SO-CALLED SPORADIC CRETINISM IN NORTH AMERICA.*

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The object of this paper is to present a study of cretinism in the United States and Canada as to its prevalence, pathology, symptomatology and treatment. The first case was reported by Jacobi in 1879. The first attempt to collect all the available data on the subject was made by William Osler in 1893, covering but eleven cases in all. This was followed by a more extensive investigation in 1897 in which he presented sixty cases. In the following year McPhedran reported seventeen cases which had occurred in Ontario alone. In 1901 John McCrae added twenty-three more cases found in Canada. These writers were of the opinion, however, that the number of cases in existence was far in excess of those reported. Murdoch in 1900, as the result of a questionnaire sent to institutions for feeble-minded throughout the country, was able to obtain information on sixteen cases, two of which, however, had already been reported by Osler. Howard, in 1907, made a statistical study of myxedema in America and collected one hundred cases, but did not deal with cretinism or cases under puberty. The next investigation was by Anders in 1918 on myxedema and cretinism, covering the period from 1905 to 1918 under the misapprehension that Howard had covered all the cases of cretinism from 1897 to 1905. Anders found 28 cases in the literature and added 43 unpublished cases obtained from institutions and other sources, but he failed to include 16 cases reported by Sill in 1905 and 41 cases by Herrman in 1914. M. B. Gordon supplemented the literature by 21 cases in 1918. Prior to the publication of Anders' article in 1920, the writer undertook this study at the request of the editor of ENDOCRINOLOGY and found additional

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case reports in the literature, which, with 5 personal unpublished cases, total 340 cases of so-called cretinism; these include the 60 of Osler. The prevalence of this disease is probably much greater than is indicated by the figures here given, as there are numerous references in the literature to cases which existed but had not been reported.

The data in this study will be primarily confined to the 280 cases reported subsequent to those by Osler.

GEOGRAPHICAL DISTRIBUTION

The locations of the 280 cases included 27 states and Canada; when the residence of the patient was not given, it was assumed to be that of the doctor reporting it.

Canada	52	Oregon	3
New York	120	Rhode Island	3
Pennsylvania	25	Maine	2
Indiana	12	Missouri	2
Ohio	10	Nebraska	2
Massachusetts	6	Arkansas	1
Minnesota	6	North Dakota	1
Virginia	6	Montana	1
Kentucky	5	Washington	1
Iowa	5	Kansas	1
California	4	Colorado	1
Maryland	3	Louisiana	1
Illinois	3	District of Columbia	1
Wisconsin	3		

It is readily seen from these figures that geographical location has no bearing upon the prevalence of this disease. Even though goiter is endemic in Canada along the St. Lawrence, in the Allegheny Valley of Pennsylvania and along the Great Lakes, not a single case of endemic cretinism was found and the incidence of so-called sporadic cretinism was no greater than in other regions.

NATIONALITY

It was very difficult to obtain statistics as to the nationality of the parents, in an endeavor to determine a foreign predominance, if any, because of the incompleteness of the data on all cases outside of New York State. Almost 50 per cent were reported from New York and Pennsylvania, two states with large foreign population. In New York City alone the cases of Herrman, Sill and Gordon, 84 in all, were known to consist of a predominating foreign element, Austrian, Russian and Italian. It is more than probable that the large foreign population in these two states accounts for the enormous excess over the other regions.

Munson studied the incidence of goiter and cretinism among the Indians of the United States and found that while goiter was of frequent occurrence among them, cretinism was rare. He states that 7 cases have been reported in which the mind was affected to a greater or less degree in persons with goiter and quotes Martin, who found a case of cretinism with a goiter in a girl of 12 years of age among the Indians of the Blackfoot Agency. He also states that Howard reported a case of an idiotic girl of about 19 years of age who had a goiter and whose mother was also goitrous.

CLASSIFICATION

Preparatory to undertaking such an investigation as this, it is necessary to have a working knowledge of some fundamentals of the underlying pathological processes existing in cretinism. Primarily, it was established by the committee of the Clinical Society of London in 1888 that in the conditions known as myxedema, sporadic cretinism, endemic cretinism, operative myxedema of animals and operative cretinism there is a pathological condition common to all, namely, the occurrence of morbid processes in the thyroid gland.

Since then very sharp controversies have raged as to the proper classification and terminology of the different forms of myxedema. Murray defines cretinism as "a condition which is due to diminished functional activity of the thyroid gland commencing before birth or in early life before 15." Osler amplifies this by calling it a "chronic condition characterized by disturbances of the growth of the skeleton and soft parts, a remarkable retardation of development, an extraordinary disproportion between the different parts of the body, and a retention of the infantile state with a corresponding lack of mental progress."

Myxedema, so designated by Ord because of the collection of what was assumed to be mucin in the subcutaneous tissues, has been studied from every conceivable angle and viewpoint by numerous observers and as a result the classifications of the disturbances due to loss of, or diminution in, thyroid secretion have been many. It is, therefore, with trepidation that the present investigator offers a new classification based upon the present study of the condition as found in America. He feels that the condition in this country is not the condition which is recognized as cretinism in Europe, that the term "sporadic cretinism" should be dispensed with, in so far as it applies to the disease in America; that cretinism should be limited to the type occurring in Europe and Asia and that the disease which is met with in this country should be considered as a separate entity, a pathological condition resulting from diminution or absence of thyroid secretion. Based upon pathological and etiological grounds, it can well be termed "childhood myxedema." The cases published in this country were reported under various terms such as: congenital cretinism, congenital myxedema, myxedema in children, infantile myxedema, sporadic

cretinism, cretinism, etc. In this study, no specific attention was paid to the term used by the original observer.

The following classification is proposed:

Myxedema—Types

1. Cretinism (Endemic).
2. Childhood myxedema (formerly called sporadic cretinism).
    a. Congenital myxedema.
    b. Infantile myxedema.
    c. Juvenile myxedema.
3. Adult myxedema.
4. Post-operative myxedema.

Congenital myxedema (also known as congenital cretinism, thyroaplasie, angeborene myoxidiotie, myxedematous idiocy, athyreosis congenita, myxedema athyreosum) has as its fundamental basis the complete absence of the thyroid gland. Pineles insists that this term shall be limited to those cases in which there has never been the slightest vestige of a thyroid gland, and that it should be considered as an anomaly of embryological development. According to this investigator, the presence of a goiter at birth, even though this goiter be composed of nothing but inert connective tissue and the thyroid thus functionless, would be enough to prevent the case from being termed congenital myxedema. The general consensus of opinion accepts this dictum, Horsley, however, claiming that this type is rare and that the children as a rule die at birth. Their appearance is typical and the characteristic bone and cartilage changes with resulting deformities are already quite far advanced at birth.

Infantile myxedema includes those cases in which the pathological disturbances in the thyroid originated before birth, but enough thyroid tissue persists to enable the child to live. The symptoms are not present at birth, but develop within the first two to five years. The thyroid gland may be either atrophied or enlarged.

Juvenile myxedema is the term given by Parker to those cases which develop symptoms of myxedema as the result of some acute infectious disease or nutritional disturbance at any time during childhood. These children are born with a normal thyroid, are normal at birth and in their subsequent mental and physical development, but following an acute disease show symptoms due to a progressive atrophy of the thyroid gland.

Infantile and juvenile myxedema differ from congenital myxedema in that they are due to pathological processes in an already existing thyroid gland, whereas in the latter the gland has never been present.

McCarrison describes another type of cretinism which he terms nervous cretinism, characterized by idiocy associated with cerebral diplegia and tetany due to congenital fibrosis of the thyroid and parathyroid glands. No cases of this type have been encountered in American literature.

Endemic cretinism is characterized by similar clinical manifestations as sporadic, but occurs only in countries where goiter is endemic. It will be dealt with more fully later on in the paper. There has not been a single case of endemic cretinism reported in the United States or Canada, and Osler considers that it is not at all probable from what he can learn that it has ever existed here.

ETIOLOGY

A question that has not as yet been settled is whether or not cretinism is a congenital disease. McCarrison claims that cretinism is always congenital, whether endemic or sporadic, except in those cases that arise postnatally from nutritional or infectional conditions. Kocher feels that "where the children are not born cretins, the thyroid gland in the majority of cretins has been congenitally so influenced that as the child grows, the sleeping abnormality in the gland begins to develop and the process continues until cretinism has been established. As can be seen, this is not strictly congenital; that is, the condition does not appear at birth and yet it is congenital because during fetal life through the blood or nourishment or drinking water or the mother, who herself may not have been a cretin and may have possessed a normal gland, the injurious tendencies were implanted in the thyroid gland of the fetus."

G. E. Smith, as a result of extensive study of fetal and maternal athyreosis among animals in goiter districts, claims that when an individual affected with thyroid disturbance becomes pregnant, unless that disturbance is counterbalanced by exceptionally favorable conditions, there will be a very seriously arrested development of the fetus, resulting in a more or less severe form of fetal athyreosis and grave disturbances will be produced in the maternal organism also. In our series in which goiter in the parents was mentioned, 13 gave a history of a goitrous mother at the time of the birth of the myxedematous child, while in 2 others, the mother developed a goiter subsequent to the birth of the affected child. In one family in which there were 12 children, the mother developed goiter after the birth of the second child, bore normal children until the birth of the patient, who was the eleventh, and then had a normal child in the twelfth pregnancy. In this instance the thyroid condition in the mother could not have been of very much etiological importance. There was no history of goiter in the father. Hodgins of Canada called Smith's attention to cases in which the father had tetany and the children had developed myxedema. McCarrison also cites the prevalence of endemic tetany in India as a disease of child-bearing women and corresponding to the locality of endemic goiter.

There are probably many cases of so-called sporadic cretins who become impregnated, but the only case on record in the literature is that reported by Townsend in 1897 and mentioned by Osler in his series. This woman was 38 years old, a typical idiot with the characteristic appearance of a cretin. A Caesarian section was performed

and a male infant was delivered. This child, while very feeble, did not show any signs of myxedema. He died in four hours. No autopsy was performed. Of course, the absence of signs of myxedema at birth would preclude the diagnosis of congenital cretinism, to use Pineles' term, still we cannot state definitely whether or not that child would have developed the disease later.

Heredity is probably a factor in the development of thyroid derangement, but it is difficult to estimate the extent of its influence. We can, however, safely state that the occurrence of but 13 cases of goiter in the mother indicates that it is probably of slight significance as an etiological factor in the production of childhood myxedema.

Tuberculosis, neuropathy, alcoholism, insanity and other degenerative strains have not been considered of much etiological importance by such investigators as Pineles, Tredgold and Murray, while Crotti and others feel that they have some bearing. Their incidence in the parents and family was small in the cases reported in America. On the mother's side there was a history of alcoholism, 2; tuberculosis, 8; insanity, 1; epilepsy, 3. On the father's side, alcoholism, 4; tuberculosis, 4; neuropathy, 1; paralysis, 1. Epilepsy, mental deficiency and goiter were found in both cousins and maternal aunts in several instances, but not of such frequency as to make them of etiological import. There were two instances of feeblemindedness not of thyroid origin in brothers and sisters.

The presence of childhood myxedema in more than one member of a family was met with several times. Sanderson and Sill each reported one instance of 3 cases in one family, and Herrman two. Manson, Niles, A. Gordon, Koplik, McPhedran, Stewart, M. B. Gordon and Murdoch all cite instances of two in a family. In all, there were 4 instances of 3 in one family and 14 of two in a family. Manson's cases were twins, while Herrman reported a case in a twin with the other child normal. In a case reported by Busey there was a marked incidence of goiter and childhood myxedema in the family; the mother, maternal grandmother, a sister and two brothers of the mother had goiter. McCrae reported a case of childhood myxedema with a goiter in which both of the patient's sisters had goiter but not myxedema.

So-called sporadic cretinism does not seem to have any special predilection for either the first born or last born in the family, for in 100 cases in which the incidence of birth was noted, it was shown that in the majority myxedema occurred in children who were both preceded and followed by normal children.

Age at Time of Reporting, Where Given

Under 1 year.....	9	6 years	11	12 years	4
1 to 2 years.....	16	7 years	8	12 to 15 years....	8
2 years	14	8 years	10	15 to 20 years....	11
3 years	10	9 years	10	20 to 30 years....	19
4 years	9	10 years	3	30 and over.....	13
5 years	13	11 years	3		

The sex of the cases where mentioned in this series, exclusive of Osler, shows the following: male, 78; female, 152—a female preponderance of 2 to 1 in keeping with the findings of Osler in America.

AGE OF INCIDENCE

The clinical manifestations of childhood myxedema depend primarily upon the amount of thyroid present and to a lesser extent upon the age of the child at the time of first appearance of the symptoms. Two, therefore, of the same physical age will present different stages of development if the disease appeared in one, say, at the age of 12 months and in the others at 8 years. Of 113 cases in which the date of first appearance of symptoms was noted the following distribution was found:

At or from birth.....	13	From 18 months to 24 months	25
From 6 weeks to 6 months...	10	From 2 years to 10 years....	16
From 6 months to 12 months	40	Over 10 years.....	2
From 12 months to 18 months	7		

There were 13 cases in which the symptoms were noted either at birth or the child appeared abnormal practically from birth. The incompleteness in the majority of cases of detailed symptomatology and the meagerness of description prevents us from considering all of these 13 cases as those of congenital myxedema. The presence of a goiter in one case automatically removes it from the congenital type to that of infantile myxedema, if we adhere to Pineles' classification. In three cases in our series, however, those of Sill, Herrman and Koplik, there seems to be no question that the condition at birth fulfilled the requirements of congenital myxedema. Osler includes one in his series, the case of Friend.

Herrman's case was that of a male whose parents were cousins. The delivery was normal. The symptoms were recognized at birth, but first observed by Herrman at 7 weeks of age. The length of the child was 50 cm., the trunk was large, the forehead low, hair dry and scanty, eyes small and placed far apart, the lips thick, nose broad and flat, cheeks soft and flabby, tongue large and thick, the neck short and thickened, thyroid not felt. The chest was well formed, the skin characteristic, the face of a stupid appearance. The temperature was 96° F.

Koplik's case was that of a female child who directly followed in birth a sister who was also myxedematous. As the first child was still under the doctor's care, he had an opportunity to observe the symptoms from birth. The delivery was normal. The child became jaundiced at four days of age and continued so for several weeks. She was short and thick set, the extremities short, but not deformed. The skin was cool to the touch but not myxedematous, the tongue large, lips puffed, neck short and thick, the head oxycephalic. The thyroid was not felt. The child had a stupid look, did not cry until teased, was apathetic and dull, even the clapping of hands failing to

attract her attention. The doctor made his diagnosis on reduced temperature, marked stupidity, peculiar conformity of the extremities as compared with the trunk, hypertrophied tongue, wrinkled skin, thick lips, coarse cry, and the improvement on thyroid medication as evidenced by the child's becoming brighter, noticing its surroundings, cooing, smiling, and by the thinning of the tongue and the normal appearance of the face. The hemoglobin at the beginning was higher than later, even though the child was placed on thyroid immediately. Koplik felt that this indicated that the anemia develops as the disease progresses, but is not present in the early stages.

The subject reported by Sill was small at birth, with short extremities, which were cold to the touch. The skin was yellow and wrinkled like an old man's and hung loosely upon the body. The nose was flat and stubbed, the eyes far apart, lips thick, tongue large. There was a fatty tumor in the supraclavicular space. The child never smiled and was very apathetic.

SYMPTOMATOLOGY

The symptomatology of a fully developed case of childhood myxedema or so-called sporadic cretinism, as evidenced by the increasing number of case reports in the literature, is well known. Once observed, the general appearance and facies will always be remembered.

Head—There is a lack of synthesis forcing the sutures and the fontaneles to remain open for a longer time than normal with a resulting larger head, and yet there is the same physiognomy as in endemic cretinism. In the latter type there is a premature synthesis of the skull with a production of a broad nose, prominent lower jaws, low forehead, prominent cheek bones and large alae nasi. Due to the early synchondrosis between the os basilare and the sphenoid bone, the basal ganglia of the brain cannot develop. The fontanelles close earlier in endemic cretinism. In keeping with the general observation, we found a late closure of the anterior fontanel in nearly every case, the latest age at closing being 10 years. In another instance, both fontanelles were still open at 5 years.

Face—There is a stupid, dull look. The shape is round, moon-shaped, with a low forehead and wrinkled skin. The nose is saddle shaped, wide at the base but short and retroussé, the alae nasi are dilated. The ears are thick and everted. The eyes are placed far apart with narrow slit-like apertures, the malar regions are prominent, cheeks flabby and hanging, the lips are thick and everted, the mouth is wide open and drooling with a protrusion of the tongue which is enlarged, but without muscular hypertrophy. The face may show eczema.

Teeth—Delay in the time of eruption of both the temporary and permanent teeth is almost general. It sometimes takes years before the first set has fully erupted and an additional longer time before the appearance of the second set. In one case the permanent teeth

did not erupt until the age of 17 and only 3 had appeared by 21. In another subject 30 years of age a few of the deciduous set were still present. The teeth in childhood myxedema are carious, brittle, short, irregular in their distribution and decay very easily.

Neck—The neck is short with lipomatous masses in the supraclavicular space.

Thorax—Flatness of the thorax is characteristic.

Abdomen—Potbelly and umbilical hernia are seen.

Extremities—The arms, legs, hands and feet are very stocky; the fingers swollen; feet short and deformed, being too broad for their length; the toes are also swollen, producing an unsteady gait. The general appearance is that of a dwarf. The extremities are cold and blue at times. Muscular co-ordination is delayed. The most advanced age at which there was reported inability to sit was 3; inability to stand, 5; and backwardness in walking, 14. The gait as a rule is clumsy and unsteady.

Skin—The skin is sallow, semi-translucent as in phlegmasia albodolens. There is edema and swelling of the subcutaneous connective tissue which is more marked in the face, tongue, lips and cheeks. This seems more pronounced in the child than in the adult and because of the softer tissues imparts a much more myxedematous appearance.

Genitals—There is lack of development of the genitals marked in both sexes with a delay in puberty. There may also be undescended testicles in the male. The oldest cases in which there were signs of delayed puberty was in a man of 30 who did not show any signs of a beard and in a woman of 20 who had not as yet menstruated. Precocious development in both the primary and secondary sex elements were noted in a few cases in both sexes.

Skeleton—The skeleton is smaller than normal, due to the persistence of the epithyseal cartilage and retardation in the ossification along the epiphyseal line. The delay in ossification is seen in the skull, and pelvis as well as limbs. The spine generally shows lordosis, but at times kyphosis.

Mentality—This ranged from a mental deficiency in the congenital myxedematous type to a slight mental aberration in the other forms. In the congenital type, the children were dull, stupid, apathetic, leading a vegetative life of eating, breathing and sleeping. They could not attend to their wants, they would sit still with neither a smile nor a cry. Others showed no signs of defective mentality in the first months, but with time it was noticed that they neither cried or if so, very little, and paid no attention to other children. In the older children of the infantile and juvenile types, backwardness in school was a prominent feature. Delinquency in talking kept apace with mental deficiency. Some did not talk at all or else gave expression to their meager thoughts in monosyllables, but never advanced to the

phrase stage. The majority of advanced cases presented a guttural, harsh voice, giving vent to incoherent speech with a limited vocabulary.

Koplik and Lichtenstein described a prominence of the antithenar eminence over the situation of the os pisiformis which they consider a part of the symptomatology of so-called cretinism. They found it in all cases of this disease under their observation and also in other conditions like microcephalic idiocy and other degenerative states. The only mention of this sign in the literature is that of Engelmann, who mentions it as one of the symptoms of cretinism, but does not state whether or not it appears in her case. This prominence is immediately adjacent to the groove which separates the palm of the hand from the forearm. It is distinctly localized to this portion of the antithenar eminence and viewed from the side rises abruptly from the above groove, giving a bayonet-like appearance. It probably represents over-development of the small muscles of the inner border of the hand attached to the os pisiformis, as well as, perhaps, an enlarged condition of this bone itself. A similar condition is seen on the foot of the domestic cat. It might be caused by the act of crawling on the floor and supporting the weight on the inner border of the hands, but it was also observed in a myxedematous child only three months of age. The authors cited consider it a congenital anomoly in degenerative children and have not seen it perfectly developed in a normal child.

The onset of symptoms is early. At birth, the child appears normal, but with time it is noted that it does not act normally, does not take well to the breast, seldom cries, is more or less dull and apathetic, is backward in teething and perhaps in crawling and in the majority of instances in talking. When the child reaches a certain age, depending upon the amount of thyroid functioning, he stops growing or else slows down for a year or two and then ceases to develop. From then on, his mentality and physical development cease to progress and he either remains at that mental age or else advances very slowly. In some instances he may even retrogress and lose all the knowledge he had formerly acquired.

In another form of childhood myxedema, the so-called juvenile myxedema, the child is born normal and functionates normally until he is attacked by some acute infectious disease or some other acute pathological condition which produces acute thyroiditis and subsequent atrophy of the thyroid gland. It seems in these cases that during this acute attack there is a call for thyroid on the part of the body which is supplied but at the expense of a diminished reserve. There were 31 instances in this series in which the onset of the symptoms could be traced to a definite time following a definite acute attack. Of this number 1 followed diphtheria; 3, scarlet fever; 6, whooping cough; 1, "fever"; 3, pneumonia; 3, gastroenteritis; 4, jaundice; 1, vaccination; 1, acute thyroiditis; 2, cholera infantum; 1, sunstroke; and 4, weaning.

The manner of onset of the symptoms differs. One child at 2 years of age could talk, stand and crawl, but following an attack of whooping cough, it became dull, inactive, and constipated; the skin became dry and harsh; the hair, which was curly, became straight and dry, and the child quickly assumed the typical myxedematous appearance. Sometimes there is first a change in disposition, followed by gradual assumption of the other symptoms. In some instances, the changes are more gradual as in one case following diphtheria at 11 months of age. The change was not noted until six months later, when the first symptom to make its appearance was decaying of the teeth and a sudden swelling of the face and body. In another case, there was a history of a so-called "cold on the lungs" at 8 months, followed by very slow development until the age of 3, when there was a permanent cessation of growth. Koplik reported 3 cases following several weeks' attacks of icterus neonatorum. The patients developed signs of myxedema at 6, 12, and 15 months, respectively.

Shields describes a case in a girl who was normal until the age of 10 months, when she had an attack of acute thyroiditis accompanied by fever, swelling of the thyroid and pressure of the trachea, but with no signs in the throat. The symptoms subsided in a week. Immediately growth and development ceased. At the age of 7 she was a typical cretin of low mentality.

Four of the cases showed signs of myxedema upon being weaned. The face broadened, nose flattened, and the subcutaneous fat increased in amount. In another case, dentition ceased and the few teeth the child had already had begun to decay. She never developed any new teeth. This would apparently indicate that mother's milk contains thyroid substance. A study of our series, however, does not bear this out. Of 20 cases designating breast feeding, it was found that 8 were at the breast at the time of the appearance of symptoms, 4 showed signs at weaning and 8 gave a history of breast feeding for periods ranging from 9 months to two and a half years with no immediate symptoms following weaning. Both Gordon and Herrman found that breast feeding had apparently no influence on infantile myxedema, for a number of their cases developed the condition while at the breast. In their large series neither reported any cases of immediate onset after the discontinuance of breast feeding.

An unusual mode of onset is described by Manson in male twins, 23 years old at the time of reporting. They were both wet nursed until 16 months of age and were apparently normal until symptoms set in. At the age of 11 years, one of them was suddenly seized with an inability to walk, was put to bed, recovered and then had a second attack six months later, which was followed by ataxia and epilepsy. The second brother did not show anything abnormal until 14 years of age, when he also developed ataxia. Both ceased growing at the time of their respective attacks and at the time of reporting, their mentality was that of half their age, corresponding to the time at

which they stopped growing physically. The thyroid was non-palpable in both.

A. Gordon describes two cases of what is evidently juvenile myxedema complicated with diabetes mellitus. The children were brothers, aged 3 and 4½ years, respectively. Both complained of thirst, ravenous appetite and abundant, frequent urination with a gradual increase in mental dullness, apathy with outbreaks of excitement in the older, puffiness of the eyelids, edematous dry skin, dry hair, and in the younger the teeth were normal, but carious in the older. The thyroid seemed to be absent in both. The mother was obese and diabetic, while the father was neuropathic. While myxedema in adults attended with glycosuria is not rare, myxedema with true diabetes mellitus is.

The total energy requirements in cretins is 18 to 25 per cent below normal as shown independently by Du Bois and Talbot. With this decreased metabolism, it is to be expected that the mortality of these children would be high and their resistance low. Packard and Hand quote several instances of the lowered resisting power of myxedematous children. Still there were 13 subjects in this series over 30 years of age, one of them reaching the age of 64 after having shown symptoms when two years old.

PATHOLOGY

According to Rushton Parker, there are three groups of cases: (a) with absence of the gland; (b) with atrophy of the gland; (c) with enlargement of the gland. A diagnosis of complete absence of the thyroid cannot be made with certainty during life. The slightest strand of connective tissue may reveal its presence by means of the microscope. Excluding Osler's cases, there were 112 in which mention was made of the condition of the gland. The terms, "absent," "not palpable" and "not felt," were used interchangeably. It was noted either absent or not felt in 100 cases, atrophied in 2 and hypertrophied in 10. Complete absence is found only in congenital myxedema. Such a case was reported by Friend in Osler's series. In apparent absence of the thyroid careful microscopic examination of sections made through the usual site of the gland or neighboring structures may reveal rudimentary alveoli or anomalies as in MacCullum and Fabian's case in a 13 year old girl. There were no signs of either the superior or inferior thyroid artery. Two large parathyroid bodies lay on each side just at the lower limit of the larynx. Below and outside of the parathyroid, on each side were found small lobulated cystic structures. At one side of the cyst in each mass was a little glandular tissue formed into acini which had scarcely any lumen. It seems unquestionable that this was thyroid tissue, although it did not resemble the normal very closely. Dense fibrous tissue, in which there were occasionally very small alveoli, was found, probably representing scanty remains of the thyroid lobes. No trace of the thyroid could be found in small sections of tissues in front of the

larynx or hyoid bone. Sections through the root of the tongue showed thyroid tissue much better preserved than that in the neck, showing numerous alveoli containing colloid. The epithelial cells were cubical, some increased in size by the enlargement of the nuclei which took on a deep stain showing a functionating gland with compensatory hypertrophy. The parathyroids were normal.

Atrophy of the gland is generally found in that sub-group described as juvenile myxedema. Parker collected 10 such cases in England. Atrophy during childhood generally follows an acute infectious disease or disturbance. Osler gives a very excellent description of the gland in this type. Packard and Hand reported some unusual findings in a case of infantile myxedema. The child was breast fed until 20 months of age. When 4 months old she had an attack of apparent loss of consciousness. At the time of death she was 6 years of age and prior to that time could not walk or talk, was apathetic and fat. Thyroid had been administered with a rapid improvement in the symptoms, but she eventually died of typhoid fever after having been sick for 5 weeks. On autopsy the alveoli in the thyroid were found to be marked off by bands of white fibrous tissue, especially about the blood vessels. The cells varied in size, acini were small, many containing no colloid whatever, the total of the colloid material being smaller in amount than the normal. There were calcareous changes in the walls of the blood vessels, the media and at times the intima and adventitia showing a formation of cavities surrounded by calcareous deposits. There was found no other mention of this change in the literature. The hypophysis and thymus were both enlarged.

There were 10 cases in this series which presented a goiter. Of Osler's 60 cases goiter was present in 7, making a total of 17 goiters in 340 cases, an incidence of 5 per cent as compared with the 44 to 60 per cent found in true endemic cretinism. In one of the cases the thyroid enlargement was noted a few days after birth, from which time it became progressively larger. In another case there was a cyst about 2 inches in diameter in the right lobe of the thyroid, with a fibrosis of the left lobe.

The blood examinations reported show anemia with a hemoglobin range from 18 to 75 per cent. There was a decrease in red blood cells; in some cases a decrease in white blood cells, at other times an increase. The differential count was practically normal.

DIAGNOSIS

The diagnosis of childhood myxedema is comparatively simple. It must not be confused with minor types of hypothyroidism on the one hand or endemic cretinism and mongolian idiocy on the other.

Differential Diagnosis

Mongolian Idiocy	*Childhood myxedema or So-Called Sporadic Cretinism*
Oblique palpebral fissure and superciliary margin.	Lids swollen, almost closing eyes.
Tongue is hacked, furrowed, beef steak appearance.	Tongue large and protruding, but not furrowed and hacked.
Lips normal in size.	Lips large and prominent.
Complexion waxy and pale.	Complexion muddy yellow.
Skin not infiltrated.	Skin infiltrated and wrinkled.
Fingers thick but tapering at the points with incurving of the little finger.	Fingers have blunt points.
Abdomen not protruding.	Abdomen protruding.
No pads of fat in supraclavicular region.	Pads of fat present in supraclavicular region.
Thyroid gland can be felt.	Thyroid cannot be felt, as a rule.
Mobile.	Less mobile, apathetic.

Differences between Childhood Myxedema and Endemic Cretinism

1. Location: Endemic cretinism, according to the majority of the students of this subject, can occur only in regions where endemic goiter prevails. Sporadic cretinism, so-called, can occur anywhere, even in endemic goitrous districts. Even though endemic goiter is prevalent in Canada along the St. Lawrence and in America along the Great Lakes, in the Alleghany Valley of Pennsylvania, in Ohio, parts of New York, Ohio and Minnesota, not a single case which can be accepted as endemic cretinism has been reported in any of these regions nor is the incidence of childhood myxedema any greater in these places.

2. Etiology: The role of the thyroid in endemic cretinism is not uniformly interpreted by all investigators. Kocher and Wagner claim that clinical manifestations of endemic cretinism are due to thyroid disturbances alone. Kutchera, Bircher and Ewald, on the other hand, think that it is due to some other factors in addition to thyroid dyscrasia, feeling that it is a physical as well as an intellectual degeneration not solely dependent upon thyroid pathology, but to some other additional damaging influences in other organs of the body as a consequence of the endemic. One of these causes is that the endemic has been exerting its influence upon the organisms of these individuals throughout successive generations, the degree of the toxicity depending upon the amount of noxious material present in the organism and also in the locality. This latter view is strengthened by the birth of endemic cretins only in endemic locations, for a goitrous mother will bear a well-developed, normal, intelligent child if she removes from the endemic territory.

The role of the thyroid in childhood myxedema or so-called sporadic cretinism has been accepted and proved.

Influence of goiter in the mother: In almost every case of endemic cretinism, there is a history of goiter in one of the parents.

In childhood myxedema, in America, there was an incidence of 13 cases of goiter in the mother and of none in the father out of a total of 340 cases, an almost negligible influence.

Psychic factors: Fright, worry, mental depression and "antenatal impressions" are reported as prominent etiological factors in the production of endemic cretinism, but are of absolutely no importance in childhood myxedema.

Illness in mother during pregnancy such as rheumatism, tetany, malaria and nutritional factors in both the mother and the child, both antenatal and postnatal, were of no etiological importance in the production of childhood myxedema in our series, but are admitted to be causative factors in the production of endemic cretinism by McCarrison and others.

3. Differences in the body skeleton: In endemic cretinism, the retardation of ossification is much more irregular than in childhood myxedema; certain epiphyses and synostoses undergo normal ossification, while others do not. There is a premature synostosis between the os basilare and the sphenoid with a consequent earlier closing of the fontanels. In the myxedema of children, the enchondrial and periosteal ossification is considerably retarded and takes place later in life. The fontanels remain open for a long time.

4. Duration of disease: In endemic cretinism, the disease remains stationary and as a result, the subjects live to an old age. Ewald makes the statement that he has never seen nor heard of a victim of sporadic cretinism living beyond the 30th year. This is based upon observations in Europe. Crotti takes the same view. That what has been called sporadic cretinism in America is probably not the same disease as that so styled in Europe may perhaps account for the finding of 13 subjects in our series who were beyond the 30th year, one still living at the age of 64 at the time of publication. Osler noted 7 past the age of 30 in his series.

5. The presence of goiter: The incidence of goiter in endemic cretinism has been rated at from 44 to 60 per cent by different observers. Pineles classifies sporadic cretinism as a sub-variety of congenital myxedema and insists that the presence of a goiter immediately stamps a case of cretinism as of the endemic type. By dispensing with the term "sporadic cretinism" for the cases observed in America, we can avoid the pitfalls of a complex terminology as to what is and what is not endemic cretinism. In our series of childhood myxedema, there were 17 cases of goiter out of a total number of 340, an incidence of but 5 per cent.

The thyroid gland in both endemic cretinism and childhood myxedema, when enlarged, may either be completely fibrosed or more commonly the gland is in a state of partial fibrosis and hyperplasia.

It may be the site of cystic enlargement or interstitial hypertrophy with a resultant non-functionating gland.

TREATMENT

In the treatment of endemic cretinism, it has been demonstrated time and again that thyroid extract is not nearly as efficacious as in the so-called sporadic type. This means that the former disease lies further back than the loss of the thyroid, both the goiter and the cretinism resulting from the same influence or else the condition is a complex one and only partly of thyroid origin.

In the treatment of childhood myxedema there is great variance as to dosage, the form of gland used and the method of administration. The dosage ranged from 3/10 grain a day to 45 grains a day of thyroid extract. Some used the powder, others the extract in tablets. To make matters still more complicated, the dose was designated as so-and-so many tablets without indicating the content of the tablets.

There can be no uniformity in the treatment of this condition until the thyroid extract used is standardized in the process of manufacturing and in the designation of dosage. While all the products must conform to the requirements of Pharmacopeias, there is no law governing the standardization of the processes of drying, defatting, and refrigerating of the original gland substance. The different methods in vogue by the various packing houses and endocrine manufacturers and the consequent products differ in many respects.

At the present time, to insure beneficial results, it is best to decide upon a certain manufacturer's product and continue to prescribe it by name, because of the variations in strength of the supposedly same dose of different firms.

The dosage seems to depend upon individual susceptibility and not upon either weight or age. The amount of thyroid that can be taken without producing toxic symptoms depends upon the amount of antogenous thyroid of the subject as well as his susceptibility to the hormone. There is no means known at present of ascertaining these, hence it is best to start with small doses and work up to the point of tolerance. The tolerance may vary from two grains of thyroid a day to more than 45 grains (Manson's case). Wood, in discussing Lamb's case, referred to a child who by mistake took 20 to 30 tablets of thyroid extract at one time without any harmful effects. He did not state the dose of each tablet. In contradistinction to this, Lamb's patient developed signs of acute thyroiditis when more than ½ grain a day was taken. When first introduced, large doses were in use, but now there seems to be a swinging toward the other extreme, for the present tendency is towards smaller doses at the onset with a gradual increase. The tolerance is thus increased, so that a child who was unable to take ½ grain at the onset can be given two or three grains within a short time. The method of some is to administer the gland on alternate weeks with intervening periods of rest, while others prescribe it

for a month and then rest. Still others advise a continual administration, with a graduatory upward dose.

The reaction produced by a dose beyond the child's tolerance is essentially that of acute thyroiditis and comprises nervous, gastro-intestinal and cardio-vascular symptoms such as extreme restlessness, crying spells, loss of sleep, vertigo, headache, diarrhea, vomiting, syncope, tachycardia, flushed face, rapid rise in temperature, falling out of the hair and general exhaustion. Upon the appearance of any untoward symptoms, the thyroid must be immediately discontinued, to be resumed only when these have disappeared. Upon resumption, it is advisable to start with a smaller dose.

The results obtained in the treatment of childhood myxedema has fully justified the hopes held out by Horsley, Murray and Mackenzie years ago. It is the one triumph of organotherapy that is unquestioned. We will not attempt to essay a statistical analysis of the results obtained in this series. Many cases were absolutely cured, others were ameliorated, while still others were not influenced at all. The outcome depends upon several factors: the amount of thyroid deficiency, the time of the onset of the treatment, the age of the patient, and the regularity with which the treatment is carried out, together with the length of time under treatment. The secret of success is early diagnosis, with early and long continued treatment. The physical defects such as those of walking, teething, crawling and bodily development are more amenable to treatment than the mental defects. In children with pronounced mental retardation, the mentality may improve to a large extent, but still never reach the normal. Some always remain a few years behind others of their age, while others develop up to a certain mental age and then remain stationary.

The initial signs of a beneficial result are generally a rise in temperature and an improvement in the appetite. There may be a preliminary loss of weight followed by an increase, with an accompanying increase in height. The child becomes brighter, shows an interest in its surroundings and in itself. The hair and skin become softer in texture and the latter loses its myxedematous appearance. The shape of the face changes. Constipation and even eneuresis are cured. Abdominal distention is reduced and sometimes umbilical hernia disappears. The blood may show an increase in the hemoglobin. Du Bois found that the total energy metabolism was raised almost to the normal on the third day of treatment.

SUMMARY AND CONCLUSIONS

1. Cretinism as it exists in Europe does not exist in America. Not a single case of true endemic cretinism has ever been reported in America. The sporadic cretinism as encountered in Europe differs from what has been termed the same disease here. There seems to be such an indefinite understanding as to just

what is meant by the term sporadic cretinism, that it seems advisable to dispense with it, at least in America, and to restrict the term cretinism to the endemic type found in Europe and Asia. The so-called sporadic cretinism of America is really an intense and exaggerated form of hypothyroidism and as such should be known by the term of childhood myxedema or myxedema in children.

2. Childhood myxedema is not uncommon in America, although there are some localities where it is not often seen. The incidence is probably greater than that indicated by the 340 cases reported in the literature. There were only 4 of the congenital myxedematous type and 31 cases of the juvenile type. The rest were of the infantile myxedematous type.

3. The greatest number of cases was found in New York and Pennsylvania. This finding is probably due to the large immigrant population in those two states. Geographical location had no apparent bearing upon the prevalence of this disease.

4. Hereditary influences appear to be of little etiological importance, although there were several instances of more than one case of childhood myxedema in the same family.

5. The incidence in females was twice as great as in males.

6. Treatment with thyroid gland products is of great though not unfailing benefit. Some cases are curable. Mental retardation is not so amenable to treatment as physical deficiency. Prognosis depends upon the age at which treatment is instituted and upon the regularity and continuance of treatment.

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THE EFFECT OF BODY TISSUES OTHER THAN THE THYROID UPON THE BASAL METABOLIC RATE

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During the past 20 years the rôle of the body tissues in regulating the basal metabolic rate of the organism as a whole has been thoroughly studied. Errors in technic and lack of careful controls have rendered much of this work unsatisfactory; but reports of great value are to be found in the literature. The thyroid gland has been more carefully studied than any other tissue, as it seems to be the gland of internal secretion which exerts the greatest regulatory influence on the rate of oxidation in the organism. So much has been written on this subject, and the reports have been so thoroughly summarized in recent articles (1) that the rôle of this gland will not be considered here. It must be understood, however, that the effects produced by extirpation of the thyroid and feeding of its active principle are usually of far greater magnitude than those ascribed in this article to other organs. Aside from effects due to the nervous mechanism (2), there are changes in the basal metabolic rate which are caused by other tissues in the body. The object of this paper is to show the present status of our knowledge of this subject by summarizing valuable work reported in the literature. In this way possible fields for further investigations may be suggested.

As there are three general types of investigation the literature falls into three groups: first, extirpation of the various organs; second, feeding of dried organs, or of their active principle; and third, injection of active principles or organ extracts. All of these experimental procedures may distort the physiological activity of organs not under immediate consideration. This factor is perhaps of least importance in the feeding experiments where surgical manipulation is not involved. But since digestion may render the active principles inert, only positive results are of value in this type of investigation. By extirpation of organs, their regulatory influence on other tissues may be

observed; but such a procedure, of course, merely demonstrates the effect of elimination and allows no opportunity for the observation of hyperactivity.* The poorest of the three methods seems to be the injection of usually very large quantities of active principles of the organs. This produces a picture which is pharmacological rather than physiological and may not really show the normal function of the organ. All three methods, therefore, have distinct limitations, but they may still give good evidence in regard to the general physiological influence of the tissues. The difficulty in studying cases of deranged internal secretion in man lies in the fact that in most cases there are pluriglandular disturbances and not sharply defined abnormalities of a single gland. Under these conditions it is quite impossible to determine the influence which each gland may be exerting.

The Pituitary. Benedict and Homans (3) removed the anterior lobe of the pituitary gland in the dog, and noted that with the deposit of fat, which began about a month after the operation, there occurred a drop in the production of CO_2 per kilo of body weight. This work was very carefully done. Some stress must be laid upon the fact that the experiment extended through many months, for when operated on the dogs were not fully grown, and probably their metabolic rate per kilo was higher than when they were adult. It is also to be noted that according to Lusk (4) the mere retention of animals in cages for long periods of time causes a reduction of their metabolic rate, though this was controlled in one of their experiments. It is, therefore, questionable whether the drop of 10 to 35 per cent in the metabolic rate per kilo is entirely due to removal of most of the hypophysis. Other evidence, however, corroborates the observation that the pituitary plays some part in the regulation of metabolism.

Aschner and Porges (5) removed the whole anterior lobe of the pituitary of a six weeks' old dog. When 10 months old the animal was small and undeveloped, with a metabolism lower than that of normal animals. For this experiment there are, however, no very good controls.

Sack (6) and Schafer (7) in studying white rats found that feeding the anterior lobe and whole gland of the pituitary had no

effect on protein metabolism. They did not study the gaseous metabolism.

In human beings, however, changes in the pituitary gland are often associated with slight effects upon the metabolic rate. Magnus Levy (8) thought these cases always associated with disturbances of other glands. Boothby (9) has observed that apparent over-functioning of the anterior pituitary may cause a rise in the metabolic rate, while hypopituitarism may be associated with a rate somewhat below normal, although there is little evidence that the secretion of any part of the gland is concerned with the normal rate of cellular combustion. Means (10) has found a reduced metabolism in cases of obesity due to hypopituitarism. Bernstein (11) found two cases of acromegaly and one of hypophyseal dystrophy in which the total metabolism fell within normal limits.

After intramuscular injection of extracts of the pituitary, Bernstein and Falta (12) observed acute changes in the respiratory metabolism. Injection of a protein-free extract of that portion of the gland which is of nervous origin,—that is, the usual pituitrin,—caused a rapid increase in oxygen consumption and an increase in CO_2 production which did not reach its maximum within three-quarters of an hour. Except for a slight rise immediately after injection the respiratory quotient did not change. There was, therefore, an increase in the metabolism after the injection, but no change in the relative percentages of the various foodstuffs burned. The blood pressure was not markedly affected. Sturgis, Wearn and Tompkins (13) tried similar experiments, using 1 c.c. of pituitrin. In eight subjects studied, seven showed no noteworthy effects in the metabolic rate, but one showed a rise of 13 per cent over the basal value. This is directly opposed to the observations of Bernstein and Falta.

Injection of the anterior lobe by Bernstein and Falta (12) showed quite a different picture. A protein-free acid extract of the glandular portion of the hypophysis was used. A short while after intramuscular injection of this extract both the CO_2 and the O_2 exchange fell markedly, the oxygen absorption decreasing the more rapidly so that at first the respiratory quotient rose sharply. This was only temporary, however, and as the

CO_2 elimination continued to fall the respiratory quotient soon reached its original level. This reduction of the basal metabolic rate lasted about an hour. On experiments such as these, however, too much stress can not be laid. The injection of such large doses of glandular extracts produces effects which probably do not represent clearly the function of the active principles during life, and which may not even be caused by the active principle. This type of work should be regarded as demonstrating the pharmacological rather than the physiological action of these tissues. These experiments have not been confirmed.

The studies of the pituitary, therefore, suggest the following conclusions:

1. Removal of the anterior lobe causes a mild reduction in the basal metabolic rate which does not develop for weeks after the operation.
2. Feeding experiments, which are not numerous, show no effect.
3. Injection of the glands has a marked influence on the metabolic rate, but the effects so produced may not indicate the usual physiological action of the glandular secretions.
4. While there is in man a tendency toward an increased metabolic rate with hyperpituitarism and toward a lowered rate with hypopituitarism, it is not clearly shown that these slight changes are caused primarily by the functional disturbances of the pituitary alone.

The Gonads. The literature on the relation of the gonads to the metabolic rate is neither very full nor very convincing. Most of the work has been done on animals before and after castration. While such studies strongly suggest that removal of the gonads causes a slow but definite reduction in the rate of metabolism, investigation of the effects of the internal secretions of the gonads in man has not clearly supported the results of animal experimentation.

Loewy and Richter (14) in their studies of the respiratory metabolism of a male and a female dog before and after castration found a decreased oxygen absorption after castration. This was more marked in the female than in the male, amounting, three weeks after operation, to a fall of 5 per cent in the metabolism per kilo of body weight. Three months after the opera-

tion a decrease of 18 per cent was found. When tablets of "oophorin" were fed to the female the metabolism rose not only to the original normal rate, but to 50 per cent above normal. Pächtner (15) is reported to have confirmed these results; but Leo Zuntz (16), who later fed oophorin to the same dog which had been experimented upon by Loewy and Richter, could obtain no such increase in the metabolic rate as they reported.

Murlin and Bailey (17) in very careful work upon two female dogs found that the distinct fall in the basal metabolic rate following castration was of very slow onset. In one dog this decrease was 17.5 per cent per kilo per hour, and in the other it was 14.2 per cent. Working on white rats, Kojima (18) also obtained a diminished metabolic rate after castration. In four male rats he found the excretion of CO_2 per kilo of body weight to be 28 per cent lower than normal three weeks after operation. Seven weeks after gonadectomy this same low rate was still maintained. Similarly, Kallestinoff (19) has shown that the nitrogenous metabolism falls after castration, but as his work is very poorly controlled but little value should be ascribed to it.

In contrast to the results of these various authors, Luethje (20) reports no difference between the respiratory exchange of normal and castrated animals. This may be perhaps because he did not use the animals upon which he later operated as controls, and because separate controls are not very satisfactory in a series of a few experiments.

That there is some interrelation of the thyroid and the sex glands in their effect upon the metabolic rate is suggested by the experiments of Rovinski (21), a pupil of Korentchewsky, who studied the effect of castration upon animals whose thyroid had previously been removed. In a long thesis published in 1913, he reports the results of experiments which indicate that although a fall in both nitrogenous and gaseous metabolism is usual after gonadectomy, it may not be constant. In the intact animal he finds this to be more marked than in thyroidectomized animals. From this Korentchewsky (22) concludes that the effects of the thyroid and the sex glands upon metabolism are synergistic, and that at least a large part of the changes following castration may be explained by the influence of the thyroid.

Leo Zuntz (23) in his experiments on the metabolism of castrated women determined the metabolic rate before and after removal of the ovaries. All the women were menstruating before the operation. In no case did he find a fall in the rate of metabolism within the first seven weeks after castration. Later there was a fall in some cases and not in others. After feeding his patients with large doses of oophorin the basal metabolism increased very slightly and thus confirmed the results he obtained by feeding oophorin to the dog upon which Loewy and Richter had worked.

In contrast to these results, Tierney (24) reports that in a patient whose pathological picture suggested pure ovarian insufficiency he found the basal metabolic rate to be 13 per cent below the average normal.* But he states that in his experience "primary gonadal insufficiencies, as a rule, have not shown such a decided decrease in the basal metabolic rate."

Snell, Ford and Rowntree (25) have published a preliminary statement in which they report a rise in the basal metabolic rate of women during menstruation,—a result which L. Zuntz (26) did not find in his two subjects. Recently Blunt and Dye (27) have studied a large series of women and have not been able to demonstrate any definite change in the basal metabolism during menstruation. They have also found no rhythmical periodic variation.

All the literature seems, therefore, to indicate that the removal of the gonads causes in animals a rather slow fall of metabolism, which amounts to about 15 per cent three weeks after castration. The view held by Korentchewsky (22) suggests that this fall may be dependent upon the presence of the thyroid gland, and that it may be due solely to the interaction of the thyroid and the sex glands. Far too little work has been done to justify us in drawing clear-cut conclusions. More cases should be studied both before and after operation in order to confirm the fact that loss or absence of the gonads causes a slight reduction of the basal metabolic rate. There should also be further work on the effects of glandular feeding and of the marital state, before any definite conclusions are drawn as to the influence of the gonads upon metabolism.

*DuBois and DuBois, also Aub and DuBois.

The Spleen. In a recent article Danoff (28), working under Asher's direction, reports the effect of removal of the spleen of white rats. Using Haldane's method to determine the respiratory metabolism, he found a rapid increase of about 50 per cent in the metabolic rate after splenectomy. This progressed until death, which, in the four animals successfully studied, occurred within ten days after the operation. It is claimed that white rats do not live longer than this after splenectomy. After the operation the animals perspired freely and the excretion of urine was markedly increased. To this work there are two objections: first, no indication of the temperature of the animals is given; and second, Danoff does not state whether the animals were active either before or after operation. In the same year that this article was published, Tomkins, Brittingham and Drinker (29) reported the results of a study of two cases of splenic involvement. One case of Banti's disease showed a metabolic rate 8 per cent above the normal of the DuBois linear formula. The other case, of splenic anemia, had a metabolic rate 5 per cent above normal before splenectomy. After removal of the spleen the metabolism of this subject was found to be 15 per cent below normal. These results are directly opposed to the findings of Danoff.

Korentschewsky (30) also studied the effect of removing the spleen in three male dogs, and could find no marked effect upon either the nitrogenous or gaseous metabolism. King (31), who did not study the respiratory metabolism, found only a slight increase in the nitrogen excretion. There were no striking changes in carbohydrate or fat absorption, or in the calcium, chloride or endogenous uric acid excretion. Most of the evidence, therefore, indicates that the spleen does not markedly influence the metabolism.

The Blood. The effect of abnormal conditions of the blood upon the metabolic rate has been studied by several investigators. In man, Kraus (32), Bohland (33), Magnus Levy (8) and Meyer and DuBois (34) have found a somewhat increased metabolic rate during anemia; but this increase is so slight as to fall almost if not quite within normal limits. Tomkins, Brittingham and Drinker (29) agree with these findings and state that the basal metabolic rate oscillates about the levels usually accepted as

normal. It therefore seems fair to conclude that even severe anemia does not markedly affect the basal metabolic rate, but may raise it slightly.

Leukemia, on the other hand, causes a very sharp increase in the metabolism as has been shown by Grafe (35), Magnus Levy (36), Kraus (32), Bohland (33), and Murphy, Means and Aub (37). This increase is about the same in both the lymphatic and myelogenous types and usually is as large as 40 to 60 per cent. At least part of this rise has been ascribed by Grafe to the high metabolism of the young white blood cells.

The Pancreas. The results obtained by the various investigators after removal of the pancreas of animals are for the most part in agreement. La Franca (38) successfully removed the pancreas of two dogs and found on the first day after operation that their respiratory metabolism had fallen. The metabolic rate began to rise after this, and was maintained for several days at varying levels far above the original basal rate. One of the dogs died of peritonitis. No reports of autopsies are given and as no figures for the nitrogen excretion are reported the D:N ratio cannot be calculated. There is, therefore, no way of determining just how completely the pancreas was removed. Verzar (39) also found that the rate of metabolism fell immediately after removal of the pancreas. Six or seven hours after the operation he shows that this decreased about 8 per cent in curarized animals, but as the operation was accompanied by a disturbance of other organs and a marked fall of blood pressure this drop in metabolism cannot be considered significant. In agreement with the results of La Franca, Murlin and Kramer (40), Falta, Grote and Staehelin (41) and also Moorehouse, Patterson and Stephenson (42) have found that the basal metabolism rises after pancreatectomy, the former authors reporting a rise as great as 42 per cent in the fasting rate. This is, of course, associated with marked changes in the relative percentages of the foodstuffs burned in the body. Carbohydrate is not utilized and the protein metabolism markedly increases. This rise in metabolism may be ascribed to the specific dynamic action of the increased protein burned rather than to any stimulation by the absence of pancreatic tissue. Therefore it is not fair to

draw the conclusion that the pancreas normally acts as a depressor of the metabolic rate.

In man the effect of diabetes upon the basal metabolic rate has not been absolutely determined. The variations observed are probably due to the types of controls and to standards of metabolism used. In mild cases it is generally agreed that the metabolic rate is normal. In severe cases, two apparently antagonistic factors are found: first, a high protein metabolism which raises the rate because of the specific dynamic action of the protein; second, the undernutrition and emaciation which tend to lower the rate. Benedict and Joslin (43) think that in their severe cases of diabetes there was an increase of 15 per cent in the metabolic rate. Lusk (44) criticized this work, and thought that the results showed only an increase of about 5 per cent. Allen and DuBois (45) found no increase even in very severe cases, while Gephart, Aub, DuBois and Lusk (46) found in severe cases of diabetes that the metabolism was reduced after prolonged fasting. In one case in which the fasting protein destruction had reached such a very high level that 27.5 grams of nitrogen were excreted per day they found that the metabolism was 15 per cent and 7 per cent above the normal rate.

The Liver. The liver plays so large a part in the metabolic activities of the organism that it is of interest to know its effects upon the general rate of metabolism. Grafe and Denecke (47) removed the liver after first making an Eck fistula. Their animals lived for four to fifteen hours after the operation. With a drop in body temperature of over 2°C., there occurred a decrease of as much as 33 per cent in the metabolism. Part of this may be accounted for by the fall of body temperature and possibly also by shock (48), although no blood pressures are recorded. The work of Mann (49) suggests, on the other hand, that this decreased metabolism may be due to an absence of glycogen and an inability normally to break down the amino acids, without the liver. According to this view, then, the liver would not be a regulator of metabolism but rather a storehouse, and the mechanism for accomplishing catabolism; and the reduced metabolism found by Grafe would be due, in part at least, to a lack of available foodstuffs. The metabolic rate of men with very severe liver disease has been shown by Aub and Means (50) to be essentially

normal; and they, therefore, conclude that in man at least the liver is not a regulator of the metabolic rate.

The Thymus. The effect of thymectomy in rabbits has recently been studied by Ruchti (51) in Asher's laboratory. He operated on four rabbits whose average age was ten weeks and obtained no evidence of clearly marked effects upon the respiratory metabolism. In his postmortem examinations he controlled his operations by microscopic inspection of sections of suspicious tissue.

The Parathyroids. Several investigators have studied the effect of removal of the parathyroids upon the basal metabolic rate. Kojima (18) found that five parathyroidectomized male rats showed no change in the CO_2 excretion per kilo of body weight thirty days after the operation. Since there was no thorough search for accessory parathyroid tissue this work is somewhat open to question, even though postmortem examination showed no accessory parathyroid tissue present in the thyroids. He also found that parathyroid feeding had no effect on the rate of metabolism. An article published two years later by Loeffler (52) reports the study of a case of chronic tetany four years after a massive thyroid extirpation. The basal metabolism in this subject was found to be 18 per cent below the average normal figures of Aub and DuBois. Part of this decrease might, of course, have been due to the lack of thyroid tissue in the body. Careful autopsy one year after the determination of the metabolic rate disclosed no parathyroid tissue although parenchymatous thyroid was present. In contrast to Loeffler's results, Rovinski (21) has demonstrated an increased metabolism in two dogs whose parathyroids were badly injured or removed during thyroidectomy. His observations were made about a month after operation at a time when the animals showed little or no tetanic tremor; but in spite of this fact and the removal of the thyroid gland, there was an increase of about 20 per cent in the nitrogenous and gaseous metabolism. Pavlov in 1913 reported in the publications of the University of Cracow the results of a study of the gaseous exchange and the metabolism after removal of the parathyroid glands, but this work is at present inaccessible (53). There is, therefore, evidence that absence of the para-

thyroids may produce every possible effect and no definite facts have been really established.

The Adrenals. Bernstein and Falta (12) have found that when 1 mgm. of adrenalin is administered subcutaneously the rapid rise of oxygen consumption which results reaches its maximum about an hour after the injection. The carbon dioxid excretion also markedly increases within the first five minutes, but then falls so gradually that it is still above normal at the end of an hour. Because of this difference in the two curves the respiratory quotient is above normal for the first twenty minutes after injection. More recent and much more complete studies have been made by Tomkins, Sturgis and Wearn (54) and by Sandiford (55). They agree that intramuscular and subcutaneous injections of adrenin invariably cause an increased heat production in normal man; and that this is usually accompanied by a rise of the respiratory quotient which suggests an increased utilization of carbohydrates.

The metabolic effects of removal of the adrenal glands of animals were first observed by Gradinescu (56). He found that the basal metabolic rate dropped markedly, but part of this fall may have been due to the lower body temperature after the operation. Aub, Bright and Forman (57) studied the effect of removal of the adrenal glands of cats. They found that even when the blood pressure and temperature were kept normal after the operation the metabolic rate fell markedly about 24 hours after adrenal extirpation. It continued, until the terminal collapse, at a level about 25 per cent below the previous normal. Their animals lived more than five days after the operation. In anesthetized animals they made observations (hitherto unpublished) that the basal metabolism decreased promptly after adrenalectomy, but that this decrease could often be eliminated by the intravenous injection of adrenalin. Marine and Bauman (58) confirmed the decrease in the metabolic rate and showed that in rabbits that survived adrenalectomy, a temporary increase in metabolism occurred approximately a week after adrenalectomy. From a few studies that have been made of the metabolism in Addison's disease it seems evident that the metabolic rate is reduced in this disease.

Whether these changes are due to the medulla or to the cortex of the adrenal glands has not been definitely established. Aub, Bright and Uridil (unpublished data) showed by removing the adrenal glands of cats that had been made toxic with thyroxin that the metabolic effects of the thyroid and adrenal glands may be independent. Since the metabolism did not return to its original level after adrenalectomy it is demonstrated that thyroxin may itself keep the rate of metabolism high. Marine (59) has shown that the injection of adrenalin may increase the metabolism even when the thyroid has been removed, and, therefore, that the effects of adrenalin may be independent of the thyroid. From these experiments it seems clear that adrenalin and thyroxin exercise mutually independent influences in increasing the metabolic rate. Here, then, are two possible mechanisms for increasing the metabolism: adrenalin, which acts quickly and for minutes only; and thyroxin, whose effect is sluggish in onset and lasts for days. These facts suggest that there may be a similar regulatory control of the metabolic rate by the two corresponding endocrine glands. In another paper this theory will be fully discussed.

SUMMARY

At present the one accurate test which indicates the activity of the glands of internal secretion is the determination of the basal metabolic rate. The activity of the thyroid gland affects this most markedly. Other tissues in the body exert some influence upon the rate, but the variations which they produce are relatively small. The greatest is found in cases of leukemia, when the basal metabolism is much above normal. In anemia there is a normal or very slightly elevated metabolic rate. Removal of the gonads often causes the metabolic rate to fall and recent investigation suggests that this may be due to some interrelation with the thyroid. Work on the pituitary suggests that hypersecretion of the anterior lobe may cause a slight rise of metabolism, although this fact is not yet well established. The adrenal gland probably has a greater effect on the metabolic rate than is generally believed. As yet this is not thoroughly explained. When the adrenals are affected, as in Addison's disease, or when both adrenal glands are removed, the metabolism is low. Injection of adrenalin is followed by a rapid increase in

the basal metabolic rate. This and other unpublished data have led to the theory that the metabolism may be regulated by two mechanisms; by the adrenals for rapid variations in rate; and by the thyroid gland for more sluggish but more important changes.

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Book Reviews

VERHANDLUNGEN DER ZWEITEN TAGUNG ÜBER VERDAUUNGS—UND STOFFWECHSELKRANKHEITEN. Berlin, 1921. Verlag von S. Karger.

This book contains the lectures and the discussions held at the second German Congress for Diseases of the Gastrointestinal tract and of Metabolism. The first three lectures on duodenal ulcer are of no endocrine interest. The fourth is an excellent review by Prof. Richter of Berlin on "Diabetes during the war." The author, though quite agreeing with those warning against over-feeding, points out that during recent years some medical men exaggerate on the other side and let their patients starve. The discussion, following this lecture, will prove useful not only to specialists, but still more to the general practitioners. The fifth lecture by Prof. Biedl on Inner secretions and Gastro-intestinal diseases has appeared in this Journal.—J. K.

BIOLOGIA DELLA VITA EMOTIVA (BIOLOGY OF THE EMOTIONAL LIFE). Vito Maria Buscaino, Bologne, 1921, Ed. Nicola Zanichelle.

Prof. Buscaino attempts to show, through experimental data, that bodily changes are not caused by emotion, but instead provoked by the same external phenomena that arouse the emotion. From a minute analysis of the so-called somatic manifestations of the emotions, he states, three general laws can be deduced. Emotion, objectively considered, results in a complex of variations, in the innervation of the striped muscles, in the parasympathetic innervation, in the sympathetic innervation, and in the endocrine system. An emotion, objectively considered, differs from another, because of the qualitative and quantitative variations in the component factors just mentioned. Certain cellular groups, with the function of which a special emotional reaction is connected, can be stimulated by peculiar chemical substances of endocrine origin, so that to a special endocrine functional variation a given emotional tonality corresponds.

A long series of experiments shows that the somatic phenomena of the emotions persist in spite of surgical or functional suppression of the brain cortex. Therefore, the somatic expression of the emotions cannot be considered as a consequence of a

subjective (cortical) variation. The encephalic zone, where the centers for the emotional reflexes belong, is constituted by the gray substances around the third ventricle and the aqueduct of Silvius (ganglia the base of the brain and mesencephalon). The psychic emotional phenomena do not arise in this zone, which rules only the somatic emotional reflexes. The subjective (cortical) emotion is a consequence of these activities.

Bringing these principles into the pathologic field the problem regarding the genesis of morbid emotionalism becomes a problem of physiology, not of psychology. We call a subject "emotional" whose subcortical centers of the vegetative affective zone are hyperexcitable. Without excepting pathologic and toxic factors, the causes of this hyperexcitability are regarded as of chemical or endocrine origin.

Emotional shock in an emotional subject arouses a very complex play of reciprocal actions and reactions between these centers and the periphery, especially in the endocrine ground, absolutely without the psychic field, and the consequences are nervous and mental disturbances.

Through an identical mechanism the psychic and nervous phenomena of hysteria and nervous shock are consequences, revealing to us the apsychic subcortico-vegetative-endocrine complex, which succeeds in dominating the mentality of the subject.

The biologic conception of the emotional life may throw light on the nature of the mental disturbances in dysphrenia, dysthymias and schyzophrenias and on the pathogenesis of dementia precox. This would be caused by an organic lesion of the vegetive-affective centers and of the cortico- and subcortico-cortical association paths.—G. V.

DALLA MEDICINA ALLA SOCIOLOGIA (FROM MEDICINE TO SOCIOLOGY). Nicolò Pende, Palermo, 1921.

The monograph is divided in two parts: 1, Endocrinology and Psychology, and 2, Vital Unity in Pathology. The first part, based on the different types determined by the predominant influence of one or another of the endocrine glands on the organism, deals especially with the mental and emotional differences shown by the various endocrine constitutions. The thyroid conditions quick mental reactions, easy and prompt association, and an emotional, changeable character. The adrenals govern the intensity of the mental (neuro-psychic) reactions, while the gonads condition a full manly development in the mental field. This is shown by the contrast between eunuchs and normal men. Moebius and Metchnikoff are quoted to the effect that creative

thought and artistic genius are strictly connected with the development of the male gonads. The pituitary gland is considered as conditioning indifferent euphoria, while its failure, according to the deductions of Timme, would be answerable for moral failure. Pende then relates various forms of delinquency described by Lombroso with endocrine abnormalities, as shown by corresponding somatic stigmata, and from this does not hesitate to postulate endocrine peculiarities as governing the differences of the human races.

In the second part the condition of the organism is said to be based on the correlation of its cellular differentiations. The studies of Levi are quoted on the growth in vitro of the cellular elements and his finding that their autonomy of growth diminishes in inverse ratio to their higher differentiation. The chemical (hormonic) stimulation accounts for the differential growth of the cells into the different organs, and the opinion of Giacomini is emphasized as regards the startling progress of the embryonal development as soon as the thyroid begins to function.

From the lowest forms of living animals, where the relative autonomy of their several elements is rather pronounced, the organic synthesis gradually increases, until it finds in man its most highly evolved expression; not even in man, however, is there absolute synthesis, as his vegetative life still preserves some autonomy. In this regard the woman and the child offer more than man an easy dissociation; and analogous ease of dissociation is also found in long exhausting disease, in puberty and in advanced age.

Some interesting examples are quoted of partial dissociation seen during the war after trifling wounds of the hand, which suddenly developed striking symptoms all along the arm, which not less suddenly gave way at the section of the sympathetic fibres of the limb.

By following all the impressions brought to our subconscious field through the sympathetic system we may find the reason for the many different emotional conditions, which could not be explained without the knowledge of the work of the sympathetic in relation to the endocrine glands.—G. V.

THE GLANDS REGULATING PERSONALITY. A STUDY OF THE GLANDS OF INTERNAL SECRETION IN RELATION TO THE TYPES OF HUMAN NATURE. Louis Berman, New York, 1921. The Macmillan Co., 300 p., 8°.

Considered as a piece of enthusiastic exposition, this book is one of the most engaging ever written in the field of endocrinology. After an introductory section dealing with adapta-

tion in relation to psychology, the author turns to endocrine physiology. Here, the instincts of the artist as distinguished from the scientist are unmistakable. Both by omission and by commission the evidence is "adapted" to the necessities of unity and balance.

For example, Cannon's theory of the emergency function of the adrenal medulla as a factor in integrative reactions, is magnified into a theory that Cannon himself has emphatically disclaimed, namely that adrenal discharge determines the reactions characteristic of strong emotion. This distorted theory thenceforth figures as a fundamental conception. The observation that the emotional reactions in question can be evoked after adrenal ablation, is ignored.

The pineal fares no better. The outstanding evidence as regards this gland is: (1) Tumors of the pineal cause precocious development (possibly by mechanical effect on contiguous nervous structures); (2) Pineal feeding causes precocious sexual and somatic development, sexual depression, or no effect, depending upon what author is consulted; (3) Pineal extirpation when performed by a skilled surgeon, such as Dandy, produces no effects, presumably because no important brain structures are injured. In the face of this evidence the author manages to reach the conclusion that the pineal controls the onset of puberty.

The thymus, which also can be completely extirpated by a skillful surgeon with no perceptible effect on the subject, becomes another important regulator of sexual development. Despite the admission that "we are a good deal at sea," "Clinical observations"—nature not stated—"emphasize that in childhood it is the chief brake upon the glands of internal secretion." This supposition is supported by the often quoted statement that the thymus reaches its greatest development at puberty. As a matter of fact this structure is much more "developed"—in comparison with the body weight, which is the essential relation—in infancy, and constantly recedes as puberty approaches, ceasing its growth when that of the rest of the body ceases.

In the discussion of the pituitary its assumed relationship to sex phenomena is emphasized despite the fact that careful researches in the laboratories of Camus and of Cushing have shown that in all probability the sexual perturbations formerly ascribed to pituitary injury are due to lesions of the neighboring brain structures.

After establishing a "physiological" background the author soars into a bizarre realm of psychologic superendocrinology. One reads many such things as "Internal secretion traits are inherited and variations in heredity are essentially the structural representations of the resultant of a parallelogram of forces exerted by each of the parental propotent glands." Some pas-

sages, however, are more lucid. One learns for instance that the complexion of his neighbor's wife differs from that of her ebony cook simply because the wife has a more efficient pair of adrenals. By the same token it would seem that a victim of Addison's disease should be regarded as a negro! Such strained deductions from analogy are frequently found not only in the book under discussion but in the writings of others who would relate anthropology and endocrine science.

In numerous instances the logic of the book will not bear analysis. Post hoc arguments are frequently employed; concomitance is treated as equivalent to causality. Dubious inferences are given the coloring of fundamental postulates. But by the use of hyperbole and of figurative diction the fallacies are skilfully thrown into the background.

With how much originality the author should be credited is difficult to determine. The ideas of Crile, Rogers and Keith are freely utilized, and readily recognized as such. Those familiar with the Italian literature will recognize also numerous conceptions previously developed by Buscaino and Pende. Considering, however, the present volume of the literature on speculative endocrinology any new theoretical conception could hardly be expected.

The work as a whole impresses the reviewer as an unfortunate piece of futility. No amount of ingenuity or enthusiasm can change the fact that we are largely ignorant of endocrine fundamentals. Pasteurs are much needed but for a Darwin, even a competent one, the time is not yet ripe. The book no doubt will command a wide circle of readers, both on account of its sensationalism and the skill with which it is written. But that it will make any lasting impression upon psychologists, to whom it is particularly addressed, is doubtful; they are trained in logic as a matter of routine. To well read endocrinologists it will be but a further addition to the list of precocious interpretive dissertations to which they have perforce had to become accustomed. That it should be taken by anyone as an exposition of present day endocrinology would be deplorable.—R. G. H.

Abstract Department

A case of ACHONDROPLASIA (Zur Kasuistik der Achondroplasie). Solotuchen, München. med. Wchnschr., 1921, **68,** 1539.

A very short note on a child of 4 with achondroplasia, which, according to the author, is due to an endocrine dysfunction.—J. K.

The autonomic nervous system and ADENOIDS (Le système nerveux végétatif chez les adénoïdiens). Ferreri (G.), Ann. d. med. navale e. coloniale (Roma), 1921, **2,** — (No. 3).

Patients having adenoids show diminution in all their vital functions, and in this condition it is interesting to study their endocrine-sympathetic system. The action of **adrenin** and of atropine as well as the oculo-cardiac reflex indicate that such patients are sympathecotonic. Sometimes one notes following tonsilectomy, a rapid loss of weight, together with enlargement of the **thyroid** gland, palpitations, gastric disorders and tachycardia—the whole amounting to a Graves' syndrome.—Presse méd., 1922, **32.**

The influence of ADRENIN on the growth of tadpoles (Ueber den Einfluss des Suprarenins auf das Wachstum der Kaulquappen). Bilski (F.), Arch. f. d. ges. Physiol. (Berlin), 1921, **191,** 108-127.

Adrenin has a growth-promoting action on tadpoles. A slight concentration is essential. Adrenin solutions, slightly changed through oxidation, are still effective.—A. T. C.

The action of ADRENALIN on the gastro-intestinal tract (L'action de l'adrenaline sur le tube gastrointestinale). Binet (L.), Presse Med. (Paris), 1918, **26,** 407-408.

From a study of the literature Binet concludes that experimental medicine has furnished evidence of digestive disturbances due to adrenal insufficiency. Among these are gastric ulcers, and vascular, secretory and motor disturbances.

Injection of ADRENALIN in an infant (Adrenalininjektion bei einem Saügling). Bliedung, Deutsche med. Wchnschr. (Berlin), 1922, **48,** 47.

In an infant cardiac arrest occurred during narcosis. Two-tenths cc. of a 1/1000 solution of adrenalin was injected into the heart with splendid success.—J. K.

Experimental modifications of the distribution of urinary nitrogen by the subcutaneous injection of ADRENALIN (Modifications

expérimentales de la repartition de l'azote urinaire par injection sous-cutanèe d'adrenaline). Brel (J.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1057-1058.

Rabbits in a good state of nourishment and normal alimentation, when injected subcutaneously with adrenalin, show a constant rise in nitrogenous relations and often a slight rise in the relation of amino nitrogen to total nitrogen. The same is often true of a fasting animal, but not always; during prolonged fasting there may be a fall of nitrogenous relations, and a slight amino-aciduria which persists until death. Animals allowed to fast, and then fed, show notable but transient disturbance of nitrogen distribution. Contrary to Noël Paton, it appears that adrenalin acts favorably on ureogenesis. Nitrogen exchange becomes more perfect because adrenalin stimulates the amino acid function of the liver.—T. C. B.

ADRENALIN in hyperglycemia. Brösamlen, Deutsch. Arch. f. klin. Med. (Leipzig), 1921, **137**, 299-310.

Adrenalin, when injected in normal persons, always causes hyperglycemia. Glycosuria is not so constant. The author only found it in a case of Graves' disease, a case of adiposity, a case of serious tuberculosis and a case of leukemia. The glucosuria began about 3 hours after the injection, reached its height in 2 hours and never lasted longer than 11 hours. The hyperglycemia begins ± 10 minutes after the injection, reaches its maximum in 1 hour; after 2 or 3 hours a slight hypoglycemia can be found. The changes in sugar metabolism begin much later than the change in blood pressure or the disagreeable feelings of the patient. In Graves' disease the hyperglycemia is more marked than in healthy persons. In one case of myxedema the amount of blood sugar showed only a small increase. In diabetes there are different reactions. In some patients the blood sugar shows only a slight increase after the injection of adrenalin, in others it first sinks to a real hypoglycemia and then slightly rises, while in a third group of patients an enormous rise the blood sugar shows only a slight increase after the injection of make a differential diagnosis between pancreatogenic and neurogenic diabetes.—J. K.

Considerable augmentation of the reaction to tuberculin by addition of ADRENALIN, and the antagonistic action of quinine and other substances (Augmentation considérable des reactions a la tuberculine par addition d'adrenaline et action antagoniste de la quinine et d'autres substances). Bouveyron (A.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 834-836.

The addition of adrenalin to tuberculin (from Institut Pasteur) causes a marked augmentation of the skin reaction. Whereas in the control there is erythema or a papule of about 4 mm. in diameter, in the tuberculin-adrenalin test the papule is livid red and 9 mm. in

diameter. It is painful and lasts for some days. On the other hand, quinine, antipyrine and pyramidon are antagonistic, and reduce the reaction to tuberculin.—T. C. B.

Studies on the conditions of activity in endocrine glands. VI. Further observations on the denervated heart in relation to ADRENAL secretion. Cannon (W. B.) & Rapport (D.), Am. J. Physiol. (Balt.), 1921, **58**, 308-337.

Further experiments to prove that the denervated heart is an indicator of adrenal secretion, and that the residual increase of heart rate after adrenal ablation is not due to rise of arterial pressure, nor to changes of venous pressure, nor to improvement of poor circulation, nor to warmer blood coming to the heart from the abdominal organs, nor to the activity of accessory adrenal tissue. The paper should be read in the original.—T. C. B.

Studies on the conditions of activity in endocrine glands. VII. The reflex center for ADRENAL secretion, and its response to excitory and inhibitory influences. Cannon (W. B.) & Rapport (D.), Am. J. Physiol. (Balt.), 1921, **58**, 338-352.

It has been shown that the adrenal medulla is subject to reflex stimulation. Two questions present themselves: Where is the reflex center? Can the secretion be inhibited, and is the mechanism central or peripheral? By suitable transections of the brain stem the authors were able to trace the reflex center for adrenal secretion to the floor of the fourth ventricle, immediately behind the corpora quadrigemina. They were able to get an increase of rate in the denervated heart by stimulating the sciatic or brachial after removal of the posterior colliculi, but a section 2 mm. farther back completely abolished the reflex. When the corpora quadrigemina and all parts anterior to them are removed, stimulation of the central end of the vagus, or of the depressor, will cause a slowing of the denervated heart by as much as 24 beats per minute. This slowing does not occur if the section is made 2 mm. back of the corpora. If reflex adrenal secretion is maintaining the denervated heart at a faster rate, central vagus stimulation will diminish the rate. The conclusion is that the reflex center for adrenal secretion at the upper edge of the fourth ventricle is subject to both excitatory and inhibitory influences.—T. C. B.

Contribution to the study of lymphogenesis. Lymphagogue action of ADRENAL preparations and of lymphatic extracts (Contributo allo studio della linfogenesi. Sull'azione linfagoga dei preparati surrenali e degli estratti linfatici). Chistoni (A.), Arch. di Fisiol. (Florence), 1921, **19**, 101-121.

Extracts of lymphatic ganglia, injected in moderate doses intravenously into dogs, produce a distinct increase of lymph flow

from the thoracic duct, the lymph possessing increased density, molecular concentration, viscosity, and electrical conductivity, and yielding increased dry residue and ash. These results are in agreement with modifications of the cellular activity. Large doses produce passage of blood and hemoglobin from capillaries to the lymph stream, and simultaneously a rapid diminution of lymph flow. Adrenal preparations also produce an increase of lymph flow, but the lymph is more dilute, with corresponding diminished density, dry residue, etc. The phenomenon is due primarily to a filtration process; hence adrenal preparations belong neither to Heidenhain's first nor second group of lymphagogues. Lymphatic gland extracts belong to the first group.—A. T. C.

ADRENALIN-lymphocytosis as a test of splenic function (Die Brauchbarkeit der Adrenalinlymphocytose zur Funktionsprüfung der Milz). Frey (W.) & Hagemann (E.), Ztschr. f. klin. Med. (Berlin), 1921, **92**, 450-465.

Twenty minutes after the injection of 1 mgm. of adrenalin lymphocytosis occurs. This is perhaps due to contraction of the spleen. The authors call the reaction positive when the absolute number of lymphocytes is increased by at least 2,500 cells. The reaction is negative when the increase is less than 1,500 cells. In all cases in which the reaction was negative there were found very marked pathological changes in the spleen. Though when the reaction is positive, changes may be present in the spleen, the follicles are always normal. This proves not only that the reaction has a practical clinical value, but that the question whether the person is "vagotonic" or "sympathicotonic" is of no importance. The lympocytosis is not observed after removal of the spleen.

The effect of injection of ADRENIN on the capacity to form antigens. Frieber (W.), Centralbl. f. Bakteriol. [etc.] (Jena), 1921, **86**, 264-267; Chem. Abst., **15**, 3677.

Frieber of Frankfurt a. M. investigated the effect of adrenin injections and of unilateral epinephrectomy on the formation of antibodies. Agglutinins and hemolysins were studied. Neither procedure led to any perceptible effect. Rabbits were used as experimental animals.—R. G. H.

(ADRENAL) Variations of the vasomotor action of the splanchnic nerve (La fonction des surrénales. III. Variations de l'action vasomotrice du nerf splanchnique). Gley (E.) & Quinquaud (A.), J. de physiol. et de pathol. gén. (Paris), 1921, **19**, 355-364.

In 25% of normal dogs the rise of blood pressure obtained by stimulating the peripheral end of the splanchnic does not show the stepped rise attributed to adrenalin production. In 75% it is present. But in neither case is the nature of the curve altered by

removal of the suprarenals. The same applies to the cat, except that the simple rise is more common. In the rabbit the double rise is never seen.—Physiol. Abst.

(ADRENINE) The relation of the exchanges between blood plasma and tissue fluids, particularly that of the fluid of the anterior chamber of the eye and the cerebro-spinal fluid. I. The sugar content and the question of combined sugar (Ueber die Wechselbeziehung zwischen Blutplasma und Gewebeflüssigkeit, insbesondere Kammerwasser und Cerebrospinalflüssigkeit). de Haan (J.) & Crevald (S. van), Biochem. Ztschr. (Berlin), 1921, **123**, 190-214.

Rabbits were used in these studies. Determinations are recorded of the sugar content of liquid from the anterior chamber of the eye, the blood plasma and the cerebro-spinal fluid. Refractometric observations are also recorded. The influence of the injection of adrenine on the relations was studied. The results demonstrate that the glucose content of tissue liquids (aqueous humor and cerebrospinal fluid) usually is less than that of the blood plasma. The opinion is expressed that the 2 former fluids can be considered as ultra-filtrates from the blood. The experiments in which artificial hyperglycemia was produced by adrenalin showed that the diffusion velocity of the plasma sugar into the other liquids studied is rather rapid and of the same order of magnitude. The sugar content of the aqueous humor first obtained differs from that of the blood as does the ultra-filtrate from serum. The liquid which is secondarily obtained contains a large amount of plasma colloids and indeed the combined sugar. Its sugar content is the same as that of plasma taken at the same time. The sugar content of the cerebro-spinal fluid is much lower than that of the blood plasma and aqueous humor. This difference is attributed to a greater sugar consumption by the brain. The sugar content of the posterior facial vein is lower than that of the carotid blood taken at the same time and is due to a difference in the uncombined sugar from which it can be concluded that this latter is used in the tissues.—F. S. H.

(ADRENAL) The effect of intraarterial injection of adrenalin upon arterial and venous blood pressure in man (Die Wirkung intraarterieller Adrenalininjektion auf den arteriellen und venösen Blutdruck beim Menschen). Hess (F. O.), Arch. f. exper. Path. u. Pharmakol. (Leipzig), 1921, **91**, 303-311.

Less disturbance of blood pressure is experienced following intraarterial injection of adrenin than after intravenous administration.—W. J. A.

(ADRENIN) The influence of vagotomy upon the excretion of sugar in the kidney (Über den Einfluss der Vagusdurchschneidung auf

die Zuckerausscheidung in der Niere). Hildebrandt (F.), Arch. f. exper. Path. u. Pharmakol. (Leipzig), 1921, **90**, 142-148.

After double vagotomy in the rabbit it is found that the threshold for the excretion of sugar in the kidney is quite materially lowered. The hyperglycemia was produced by injections of adrenalin. It is held that the vagus normally exerts a direct nervous influence upon the sugar-excretory function of the kidneys.—W. J. A.

Cancer of ADRENALS. Hoffman, Deutsche. med. Wchnschr. (Berlin), 1921, **47**, 1348.

A woman with cancer of a bronchus got a cancer of both adrenals. No Addison symptoms developed. In this case the severe diarrhea was considered as due to the loss of functions of the adrenals.—J. K.

Blood acetone bodies after the injection of small amounts of ADRENALIN chloride. Hubbard (R. S.) & Wright (F. R.), J. Biol. Chem. (Balt.), 1921, **49**, 385-388.

An increase in the acetone bodies of the blood is observed after the injection of adrenaline which does not seem to bear any relationship to changes in the blood sugar. The reaction is explained on the effect of the local restrictions in blood supply induced by the drug leading to the local production or failure of combustion of the acetone bodies. The production of these bodies is not looked on as being responsible in these experiments for the marked lowering of the alkali reserve observed.—F. S. H.

Pharmacodynamic study of ADRENALONE. Vasoconstrictor and respiratory action; secretory effects (Étude pharmacodynamique de l'adrénalone. Action vasoconstrictive et respiratoire; effets sécrétoires). Jaeger (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 432-433.

Adrenalone, $C_6H_3(OH)_2$-CO-CH_2-NH-CH_3, is an intermediate product in the preparation of synthetic adrenalin, and differs from it in having a ketone group, CO, in place of the CHOH. The author supplements the work of Loewi and Mayer, and Barger and Dale, filling in certain gaps. Experiments were made on dogs anesthetized with chloralose or chloralose and atropine. The conclusions are: that qualitatively adrenalone has an action similar to adrenalin—intense vasoconstriction with rise of blood pressure, augmentation and acceleration of the heart. The effects are proportional to the dose. The intensity of its action, measured by variations in arterial pressure, is 200-220 times weaker than adrenalin. The action of adrenalone is more prolonged, due probably to the fact that it is less easily oxidized and therefore not so easily destroyed in the body. The respiratory action of adrenalone is not identical with adrenalin.

There is no long period of apnoea, but short arrests of respiration, or only relaxation; this becomes more and more intense, lasts a long time, and the respiratory movements are profound and regular. Salivary and pancreatic secretions are increased, and the urine contains sugar, which lasts until the following day. The urine is abundant and gives the Vulpian reaction.—T. C. B.

Pharmacodynamic study of ADRENALONE. Seat of vasoconstrictor action and effects of adrenalone in the presence of various vasomotor drugs (Étude pharmacodynamique de l'adrénalone. Siège de l'action vasoconstrictive et effets de l'adrénalone en présence de diverses drogues vasomotrices). Jaeger (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 910-912.

Like that of adrenalin, the seat of the vasoconstrictor action of adrenalone is the peripheral terminations of the sympathetic. Adrenalone is antagonistic to the vasodilators. After ergotinin, while adrenalin is exclusively hypotensive, adrenalone causes a transient hypotension, followed by the normal hypertensive effect.—T. C. B.

Intracardial injection of ADRENALIN in acute paralysis of the heart (Intrakardiale Adrenalininjektion bei akuter Herzlähmung). Kneier (G.), Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1490-1491.

In two cases of asphyxial cardiac arrest, adrenalin was injected into the heart. In one case no effect was seen; in the other the patient lived 18 days.—J. K.

(ADRENIN, PITUITRIN) The significance of calcium for the irritability of the sympathetic nerve endings in the heart (Ueber die Bedeutung des Calciums für die Erregbarkeit der sympathischen Herznervenendigungen). Kolm (Richard) & Pick (Ernst P.), Arch. f. d. ges. Physiol. (Berlin), 1921, **189**, 137-143. **Inverted heart-actions of parasympathetic poisons (Ueber inverse Herzwirkungen parasympathetischen Gifte).** Kolm (R.) & Pick (E. P.), Arch. f. d. ges. Physiol. (Berlin), 1921, **190**, 108-117.

(Cf. Endocrinology, **5**, 484). Vagus poisons (acetylcholine, muscarine, and pituitrin) produce no diastolic standstill in the isolated hearts of summer frogs immersed in a Ringer's solution rich in calcium ions. Winter frogs under the same conditions behave normally. The three poisons release a ventricular contracture in hearts of summer frogs previously treated with Ringer's solution containing excess of calcium and little or no potassium. Atropine does not prevent the contracture (with acetylcholine) nor abolish it. It is therefore independent of the vagus nerve endings. It is not produced after action of ergotamine on the sympathetic heart nerves, and therefore is produced by stimulation of the sympathetic whose irrita-

bility is increased through calcium action. Similar results are obtained with adrenaline.—A. T. C.

ADRENAL extirpation for epilepsy (Exstirpation der linken Nebenniere wegen schwerer Epilepsie). Kulenkampff, Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1543.

Describes the technic of the operation.—J. K.

ADRENIN treatment of rickets (Behandlung der Rachitis mit Adrenalin). Lehnerdt (T.) & Weinberg (H.), München. med. Wchnschr., 1921, **69**, 1482-1484.

The authors recommend subcutaneous injections of suprarenin hydrochlorid 3-4 times daily in doses of 0.2 cc. of a 0.1% solution. The doses must be gradually raised to 0.5 cc. A calcium preparation must be given together with the adrenalin treatment. The local anaemia, the palor, the influence on the pulse which are seen after the injections are of no consequence. Often, even in very serious cases, a marked improvement in the psychic as well as the physical condition is seen within the first week of treatment. It is advisable to treat children in this way only in a hospital.—J. K.

(ADRENALS) Sensitivity of decapsulated rats to toxic substances (Sensibilité des rats acapsulés envers les toxiques). Lewis (J. T.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 685-686.

The susceptibility of decapsulated rats toward morphine is attenuated after a certain time. In a previous note the author has affirmed that rats with unilateral decapsulation showed a diminished resistance to morphine. Further observation shows that such rats resist as well as the controls.—T. C. B.

Action of ADRENALIN on the curve of hypercalcemia (Action de l'adrénaline sur la courbe hypercalcémique). Munoz (J. M.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 954-955.

The injection of calcium chloride intravenously in dogs is followed by a hypercalcemia which lasts for 3 to 6 hours and then falls below normal, lasting 24 hours or more. Repeated injections of adrenalin do not modify the curve of serum calcium, but the total calcium did not fall below normal in five dogs thus treated, while there was a fall in the controls.—T. C. B.

The action of ADRENALIN on blood-sugar (Ueber die Wirkung des Adrenalins auf den Blutzucker). Petenyi (G.) & Lax (H.), Biochem. Ztschr. (Berlin), 1921, **125**, 272-282.

In a series of controlled experiments it was found that in man, after the subcutaneous adrenalin injection, the hyperglycemia is regularly followed by a hypoglycemia. The normal blood-sugar

values show greater variability in cases of tetany than in healthy individuals, and when adrenalin is injected the hyperglycemia is usually less, eventually dies away to a hypoglycemia of greater and more lasting degree, even when hyperglycemia does not appear a hypoglycemia is induced. Adrenalin hyperglycemia is hence considered to be only a partial expression of a very complicated process, the hypoglycemic stage can not be considered as a glycogen deprivation and is in certain cases independent of the hyperglycemia.
—F. S. H.

Changes in the ADRENALS in infectious diseases (Nebennierenveränderungen bei Infektionskrankheiten). Photakis (B.), Berl. klin. Wchnschr., 1921, **58**, 1325-1326.

In all kinds of infectious diseases (influenza, dysentery, typhoid, etc.) all kinds of changes may be found in the adrenals. Degenerations, hypertrophy as well as atrophy or necrosis are met with. What changes are found depend largely upon the intensity and the duration of the disease. It is possible to diagnose postmortem the hyper- or hypo-function of the adrenals. This diagnosis is more certain than the clinical one, as little is known of the function of the adrenals.—J. K.

Antagonism between hypotensive organ extracts and ADRENALIN (L'azione antagonistica fra le sostanze ipotensive degli estratti d'organi l'adrenalina). Pugliese (A.), Biochem. e. terap. sper. (Milano), 1921, **8**, 65-69.

Contrary to the claims of Marfori and Chistoni that in "lymphoganglin" alone a hypotensive action antagonistic to the action of adrenalin is found, the author thinks that other organs also may exert analogous action. His present experiments were made with liver extract with the following results: By injecting into the crural vein of a dog equal parts of adrenalin and of liver extract the characteristic action of adrenalin is strongly reduced; an enucleated eye dropped in liver extract undergoes accentuated myosis; myosis is also obtained in the eye of the dog and the rabbit with a few drops of liver extract; there is no mydriasis when adrenalin mixed with liver extract is dropped into the conjuntival sac of the dog or rabbit. (For further discussion see Vincent, Endocrin., **2**, 420-430.)—G. V.

The glycogen content of the tissues of diabetic animals and the influence of ADRENALIN thereon. Ringer (A. I.), Dubin (H.) & Frankel (F. H.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, **19**, 92-97.

In thirteen dogs rendered diabetic by phlorizin it was found that the muscles continued to retain a certain amount of "residual" glycogen. It amounted to 0.150 per cent even after seven days of

fasting and repeated doses of the drug. In five dogs it was ascertained that the residual glycogen could be completely driven out by means of adrenalin. Other details of interest to students of carbohydrate metabolism are included.—R. G. H.

The effect of ADRENALIN upon respiration. Roberts (Ff.), J. Physiol. (Lond.), 1921, **55**, 346-355.

The common supposition that the respiratory variations caused by adrenalin are due to its direct action on the respiratory center is hypothetical. This study is an attempt to clear up the matter. Methods are given. The conclusion is that large doses of adrenalin cause diminution and temporary arrest of respiration, with alterations of rate, and that the effect is caused by anemia of the respiratory center due to vasoconstriction. There is no evidence that adrenalin causes afferent impulses from the periphery.—T. C. B.

ADRENAL insufficiency in the light of modern physiology (L'insuffisance surrénale devant les récentes critiques des physiologistes). Sergent (E.), Presse méd. (Paris), 1921, 813-816.

A general article the nature of which is indicated in the caption. It is pointed out that the clinical conception of adrenal insufficiency does not imply, as many have assumed, a deficiency in adrenin secretion. Such phenomena as muscular and circulatory asthenia may be ascribed largely or entirely to adrenal cortex deficiency. In short, adrenin pharmacodynamics seem not to afford pertinent evidence. The abstractor would add, however, that this does not necessarily exclude adrenin as a factor in "adrenal insufficiency." Recent investigators have shown that as little as 0.5 mgm. of adrenin administered subcutaneously produces material augmentation of basal metabolism over a considerable period of time.—R. G. H.

EPINEPHRINURIA in normal pregnancy and puerperium (Adrenalinuria in gravadanza e puerperio normali). Sestini (C.), Ann. di obstet. (Milano), 1920, —, — (No. 3); Folia gynaec (Pavia), 1920, **42**, 137-152; Abst., Pathologica (Genova), 1921, **13**, 25.

Epinephrinuria in normal pregnancy is generally very intense, especially after the third month; its intensity is in direct relation to the pigmentation. Nursing puerperae show also adrenalin in the urine during the whole period of lactation, though there is no relation to pigmentation. When the puerpera does not nurse her infant there is no epinephrinuria. Newly born children constantly offer a negative reaction.—G. V.

On the mode of action of ADRENALIN and of acids, against bacterial toxins (Du mode d'action de l'adrenaline et des acides vis-a-vis des toxines bacteriènnes). Tawara (S.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 401-402.

Using mice as the experimental animals Tawara has been unable to get the results reported by Marie. All the animals died from a lethal dose of tetanus toxin, notwithstanding adrenalin in varying doses was injected at different times, from immediately after injection of the toxin to 3 hours later. Glucose solutions, after the method of Tachigara in rabbits, gave negative results. When the toxin was mixed with adrenalin before injection, however, the mice survived after 2.5 lethal doses. Adrenalin is acid and this is the cause of the neutralization. Distilled water was made acid by HCl and boric acid, corresponding to the acidity of the adrenalin. When this was mixed with tetanus toxin it had the same neutralizing effect as adrenalin. Various acids were tried and the neutralizing effect was found to depend on the dissosiation of H; HCl being the strongest, and boric acid the weakest.—T. C. B.

Experimental dissociation of the vasoconstrictor effects and ADRENALIN secretion effects of excitation of the splanchnic (Dissociation expérimentale des effets vasoconstricteurs et adrénalins-secréteurs de l'excitation splanchnique). Tournade (A.), & Chabrol (M.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 651-654.

Excitation of the peripheral end of the splanchnic nerve causes a rise of arterial pressure, but it is a question whether it is a direct vasoconstrictor action, or indirect by causing the adrenals to secrete. To solve this question an anastomosis was formed between the right lumbo-capsular vein of one dog (B), and the jugular of another dog (A). The secretion of the right adrenal of "B" is thus diverted into the circulation of "A." The carotid pressure of both animals was registered. When the peripheral end of the right splanchnic of "B" was stimulated, after a latent period of eleven seconds the carotid pressure of "A" showed a rise typical of adrenalin, while hardly a second elapsed before the carotid pressure of "B" began to rise. The effects lasted forty to fifty seconds after cessation of the stimulus. The splanchnic, therefore, has a double action—vasoconstrictor and secretory, and in the normal subject these are merged in a common action, hypertension.—T. C. B.

(ADRENIN) Contributions to the physiology of the blood vessels. I. The influence exerted by physiological fluids on the vasoconstriction produced by chemical or electrical stimuli. II. Diverse methods of action of chemical stimuli applied externally or internally to the artery. Importance of the tunica interna, and functional connections between the various vessel structures (Contributo alla fisiologica dei vasi sanguiferi. I. Della influenza esercitata da liquidi fisiologici sulla vaso-constrazione da stimoli chimici od elettrici. II. Del diverso modo di agire degli stimoli chimici applicati esternamente o internamente alle arteria. Im-

portanza della tunica interna e connessioni funziolali tra le varie strutture vasali). Vernono (Guido), Arch. di Fisiol. (Florence), 1921, **19**, 123-162.

Rabbit blood-serum increases the effect of adrenalin on the vascular system of frogs with an artificial circulation. Rabbit or horse blood-serum favors and increases the contraction of rings of calf-arteries produced by adrenalin, barium chloride, or nicotin. Adrenalin, brought into contact with the external surface of an isolated strip of artery, produces no contraction, even in large doses, while minimal doses produce an immediate contraction when applied to the internal surface. Barium chloride produces a contraction when applied internally (immediate action) or externally (gradual action). Pericardial fluid bathing the internal surface of the artery favors the action of both adrenalin and barium. It is considered that adrenalin applied externally is destroyed before it reaches the neuro-muscular junctions, while the results indicate that barium produces a mixed excitation, direct muscular, and neuromuscular.
—A. T. C.

On the excitability of the splanchnic nerve and on the movements of the intestine, after ablation of the ADRENALS (Sur l'excitabilité du nerf splanchnique et sur les mouvements de l'intestin après l'ablation des surrénales). Wertheimer (E.) & Duvillier (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 997-998.

The authors believe that the excitability of the sympathetic is maintained by the secretion from the adrenals. There is no doubt that the nerve possesses an excitability of its own, independent of that conferred on it by the adrenalin in the blood. So far as is known these observations have not been extended to the splanchnic fibers that inhibit movements of the intestine. Do these fibers preserve their activity after adrenal ablation? The experiments were made on dogs for the most part, but two cats were also used. The results were clear. Some hours after the operation, excitation of the nerve caused relaxation of the intestine and arrested its movements. When the blood pressure falls very low it occasionally happens that the inhibitor fibers survive the vasomotor; excitation then causes relaxation of the intestine, without a rise of blood pressure. It has been reported that the isolated duodenum of the rabbit after epinephrectomy contracts very feebly or not at all in Tyrode's solution. In dogs and cats the contractions are just as vigorous as in the intact animal.—T. C. B.

AMENORRHEA. Novak (J.) & Graff (E), Ztschr. f. Geb. u. Gynäk. (Stuttgart), 1921, **83**, 289-313; Abst. J. Am. M. Ass. (Chicago), 1921.

The authors found that curetting aided in restoration of menstruation in a large number of their 111 cases of amenorrhea in

women between 15 and 39. The uterus mucosa undergoes cyclic changes even without the menstrual hemorrhage. The scraps obtained by curetting show whether the mucosa is comparatively normal or atrophied, thus affording a basis for prognosis. They discovered by this means in six cases a tuberculous process in the uterine mucous membrane which had never induced any appreciable symptoms.—E. N.

Pharmacology of the AUTONOMIC system (Untersuchungen über die pharmakologische Prüfung des vegetativen Nervensystems). Rusznyák (S.), Wiener klin. Wchnschr., 1921, **34**, 591-592.

The author examined the influence of drugs (pilocarpin) on the pupil in several persons. He found that hypersensibility for adrenalin does not mean sympathicotonia. There are persons who have a hypersensibility as well for pilocarpin as for adrenalin. One organ may have a hypersensibility for one of these drugs whilst another organ of the same person a hypersensibility for the other drug. Therefore, the words **vagotonia** and **sympathicotonia** are of no significance and do not indicate a real clinical entity. The pharmacological testing of the involuntary nervous system is not reliable. —J. K.

Do drugs acting upon the autonomic system influence the leucocytic picture (Wirkt die pharmakologische Beeinflussung des vegetativen Nervensystems auf das weisze Blutbild)? Wollenberg (H.), Ztschr. f. klin. Med. (Berlin), 1921, **92**, 249-257.

Pilocarpin produces in patients with a sensitive "eosinophil system" slight eosinophilia. **Adrenalin** produces a decrease in the number of eosinophil cells in the peripheral blood together with lymphocytosis, due to migration of cells from the tissues into the blood. Then an increased number of neutrophil cells is seen. This is caused by an influence of the adrenalin upon the bone marrow. Atropin has no influence on the blood picture. It is probable that the influence of drugs on the blood picture is not caused by their influence on the involuntary nervous system, as there is no parallelism between the intensity of the change of the activity in this system and the changes in the blood picture.—J. K.

Hypertonia and BLOOD SUGAR (Hypertonie und Blutzucker). Härle (F.), Ztschr. f. klin. Med. (Berlin), 1921, **92**, 124-133.

In Bright's disease with as well as without hypertonia the blood sugar, though often rather high, nearly always remains within the normal limits. Real hyperglycemia is very rare. The contrary is, however, seen in hypertonia without changes in the kidneys. Here hyperglycemia is often met with. A parallelism between blood pressure and amount of blood sugar does not exist.—J. K.

CHOLIN as hormone of intestinal peristalsis. V. Experimental therapy of stomach-intestine paralysis after chloroform narcosis (Cholin als Hormon der Darmbewegung. V. Experimentelle Therapie der Magen-Darmlähmung nach Chloroformnarkose). von Kühlewein (M.), Arch. f. d. ges. Physiol. (Berlin), 1921, **191**, 99-107.

A 2-hour deep chloroform narcosis produces in cats paralysis of stomach and intestinal movements with all the characteristic appearances of post-narcotic gastrointestinal paralysis seen in man. This paralysis remains complete for two hours and is still noticeable after 20 hours. Intravenous injection of cholin HCl (0.005 to 0.015 gm. per kilo) has a beneficial effect on the paralysis in cats, and their general condition, the effect extending to the large intestine, and defecation being induced. When slowly injected cholin in the dosage used produces no harmful effects. The cholin-content of the cat's small intestine is not decreased by the chloroform narcosis.—A. T. C.

CHOLINE as hormone of intestinal peristalsis. III. Participation of choline in the action of different organic acids on the intestine (Cholin als Hormon der Darmbewegung. III. Die Beteiligung des Cholins an der Wirkung verschiedener organischer Saüren auf den Darm). Le Heux (J. W.), Arch. f. d. ges. Physiol. (Berlin), 1921, **190**, 280-300.

(Cf. Endocrinology, **5**, 247). Equivalent amounts of the sodium salts of formic, propionic, n-butyric, isovalerianic, succinic, pyroracemic, and benzoic acids have been tested on surviving rabbit intestine. Salts of succinic and benzoic acids have little action, and their choline-esters not much more. The others stimulate the intestine in varying degrees; their choline-esters produce a greater or less action than that of choline itself, parallel to the action of the salts. The stimulative action of the salts on the intestine fails if choline is previously removed from the intestine by washing. Atropine antagonises the action of the choline-esters, and also, similarly, that of the salts. The results suggest the conclusion that these salts form with choline present in the intestinal wall choline-esters through the agency of a synthetic enzyme; these act more strongly than choline itself, and thus favor its action. If Neukirch and Rona's theory be correct, that certain sugars which stimulate intestinal peristalsis are broken down through the stage of pyroracemic acid, then the action of the sugar is due to the intermediate production of the choline-ester of this acid, and not through sugar-combustion setting free energy for the increased muscle-work.

—A. T. C.

CHOLINE as hormone of intestinal peristalsis. IV. The influence of choline on normal stomach- and intestine-peristalsis (Cholin als Hormon der Darmbewegung. IV. Ueber den Einfluss des Cholins

auf die normale Magen-Darmbewegung). Le Heux (J. W.), Arch. f. d. ges. Physiol. (Berlin), 1921, **190**, 301-310.

The effect of choline on normal stomach and intestinal peristalsis in intact cats has been studied by Roentgen rays after intravenous injections of 4 to 10 mg. choline-hydrochloride, amounts which the cats withstood well. Antrum peristalsis was strengthened, the waves increasing in depth and number. Passage of stomach contents into the intestine could be seen frequently. The small intestine filled more rapidly, and the stomach became empty somewhat sooner than normally. The pendular peristalsis of the small intestine was increased and followed by marked rhythmic segmentation of its contents. As a result the contents had passed almost completely into the large intestine at a time when normally the small intestine was only half emptied. There was no visible increase in the movements of the large intestine. The experiments show that when the choline content of the body is slightly increased, the choline action is increased for some hours, and the period of digestion is markedly shortened. The peristalsis remains normal in kind, there being simply an acceleration of transport of contents with no abnormal appearances.—A. T. C.

LUTEUM EXTRACT: A further report. Leighton (A. P.), Am. J. Obst. & Gyn. (St. Louis), 1921, **2**, 613-619.

The paper, which is along rather general lines, is based on an experience with over 300 cases in which ovarian organotherapy was employed. The author has employed thyroid in conjunction with luteum extract in some cases of **menorrhagia**, where pelvic disease could be ruled out. He states that "more often than not exceptional benefit has followed." He also advocates luteum extract in **"dysmenorrhea** of a certain type," **hyperthyroidism, menopausal** symptoms, sick headaches at the menstrual periods, chlorosis (together with hematinics), functional **amenorrhea** and **hypothyroid obesity.** In over half of the 300 or more women treated, the indication lay in menopausal symptoms. Of the entire number, there were not over a dozen who could not report exceptional benefit even to absolute relief. The paper, it will be seen, is of a decidedly optimistic tone, the indications for the organotherapy being more often empiric than pharmacodynamic.—E. N.

Action exerecised by the CORPUS LUTEM on the maturation of follicles and on rut in the rabbit (Action exercée par le corps jaune sur la maturation des follicles et sur la chaleur de la lapine). Nielsen (F.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 614-615.

From experiments in extirpating the corpora lutea in various sexual periods the conclusion is drawn that, admitting that development and maturity of the follicles is not without importance in the

production of rut, it represents only one factor in a complex, in female mammals.—T. C. B.

CORPUS LUTEUM extract in the vomiting of pregnancy. Quigley (J. K.), Med. Rec. (New York), 1919, **95**, 982.

This is a very brief report of 17 cases. Twelve were permanently benefited, and 4 were benefited with later relapse. In these the author believes that not enough of the extract was given. There was one complete failure. The average number of doses was 7. The preparation used was in the form of 1 c.c. ampoules, containing 0.2 mg. of desiccated gland substance.—E. N.

Ova, CORPUS LUTEUM, menstruation cycle and the genesis of myoma (Primat der Eizelle, Corpus luteum, Menstruationzyklus und Genese der Myome). Seitz (L.), Arch. f. Gynäk. (Berlin), 1921, **115**, 1-14.

A dissertation the conclusions of which are that the theca-lutein cells and the follicular cells have according to their origin and function a high degree of individuality and grow and increase after the expulsion of the ovum from the follicle independently of the egg by virtue of their inherent energy, and freed from the raised intrafollicular pressure, form the temporary internal secretory gland of the corpus luteum. The cells of the corpus luteum, when the ovum is not fertilized, live from 14 to 20 days after the follicular rupture. They condition the ovarian and menstrual cycles. The corpus luteum and the premenstrual swollen uterine mucosa induced by its activity, have an indifferent period of from 14 to 20 days duration, which is independent of the life, death or fertilization of the ovum. Ovarian hormones are considered in the etiology of myoma.—F. S. H.

The liver in DIABETES MELLITUS. Bate (R. A.), Am. Med. (N. York), 1918, n.s. **13**, 220-226.

This article is based upon a reading of endocrinologic literature, much of it of questionable variety, and not upon original researches. The author tosses about statements concerning the liver, pancreas, parathyroids, hypophysis, adrenals, spleen, hormones, etc., with all the assurance of an experienced juggler. He passes from general and sometimes fantastic premises to the most startling conclusions with the dexterity of a prestidigitator, so that it is not always possible to comprehend the inner mechanism of his syncopated syllogisms.—J. P. S.

Observations on the blood fat in DIABETES. Blatherwick (N. R.), J. Biol. Chem. (Balt.), 1921, **49**, 193-199.

A study of blood fat in relation to the fat in the diet shows that subjects of mild and moderate diabetes are apparently able to utilize

satisfactorily large amounts of fat, as indicated by constancy of the blood fat level and by the absence of acetone bodies in the urine.
—F. S. H.

Certain aspects of DIABETES. Brown (W. L.), St. Barth. Hosp. J. (London), 1918-1919, **26**, 104-106.

A brief review with no new data.—F. S. H.

The value of saccharin as a food in DIABETES. Burge (W. E.), Med. Rec. (N. York), 1918, **94**, 1071-1072.

Burge determined the effect of feeding saccharin to dogs rendered diabetic by pancreatectomy. This feeding caused an increase of from 42 to 49 per cent in the catalase present in the blood. Similar results were obtained in human subjects suffering from this disease. Burge, therefore, believes that saccharin, in addition to being a sweetening agent, serves to facilitate oxidation and may be positively helpful in diabetes, in which oxidation is defective.
—J. P. S.

Experimental foundation of the treatment of DIABETES by physical exercise (Die experimentellen Grundlagen einer Arbeitstheorie des Diabetes). Bürger (H.), Therap. Halbmonatsh. (Berlin), 1921, **35**, 622-628.

The author found that physical work in healthy individuals causes a lowering of the blood sugar. The lowest content was found ± 3 hours after the work was finished. The diminution is often preceded by an increase which may be 38% of the normal blood sugar. When dextrose is injected in normal individuals much less is excreted in the urine during work than during rest. It is very remarkable that if during some days a diet without carbohydrate is given physical work causes a very marked hyperglycemia. The intensity of all these reactions largely depends upon the irritability of the nervous system. The reaction is more intense when the patient is not used to the work. By systematic exercise it gradually becomes less marked. A systematic treatment of diabetes with exactly measured muscular exercise may be useful.—J. K.

Gangrene of the limbs in DIABETES (La gangréne des membres chez les diabétiques). Ducassy (M.), Thèse de Paris, 1921.

In some cases of gangrene in diabetes the cause is a bacterial infection the extreme severity of which is caused by the large quantity of sugar in the tissues. There are, however, many cases in which the pathological changes are identical with those seen in Bright's disease, syphilis, etc., and where it is only a matter of gangrene in a case of diabetes, and not diabetic gangrene. Only the septic moist gangrene has a definite relation to the hyperglycemia, as such.—J. K.

DIABETES mellitus and hemorrhagic diathesis (Diabetes mellitus und hämorrhagische Diathese). Gorke (H.), München. med. Wchnschr., 1921, **68**, 1324.

A woman of 57 developed simultaneously a diabetes and a purpura hemorrhagica which had given rise to anemia and cachexia. Treatment of the diabetes had also a good influence on the purpura. It is believed that in these cases the purpura is due to a lesion of the endothelium, produced by the hyperglycemia.—J. K.

The duration of fatal cases of DIABETES (Die Dauer der letal verlaufenden Diabetesfälle). Heiberg (K. A.), Ztschr. f. klin. Med. (Berlin), 1921, **92**, 76-77.

The duration of fatal diabetes is much longer in elderly than in young people. It is also longer in men than in women.—J. K.

Blood pressure in DIABETES (Über den Blutdruck bei Diabetes mellitus). Hitzenberger (K.), Wiener Arch. f. inn Med., 1921, **2**, 461.

In young patients with diabetes the blood pressure is often lower than in normal individuals of the same age; in old patients it is generally higher.—J. K.

Hypertonia and DIABETES (Hypertonie und Zuckerkrankheit). Kylin (E.), Zentralbl. f. inn. Med. (Leipzig), 1921, **42**, 873-877.

There are two forms of hypertonia—that with and that without high capillary pressure. Krogh has shown that the arteries and capillaries have independent innervation. In young diabetics the blood pressure is generally normal; in the elderly it is generally high. Perhaps diabetes with and that without hypertonia have different endocrine origins. It is well known that in most cases of hypertonia there is no diabetes, but nevertheless, many patients with hypertonia show low carbohydrate tolerance. It has been stated that hyperglycemia is always present in hypertonia, but Kylin could not confirm this. Probably there are relations between hypertonia and diabetes though they are not known. It is remarkable that in **Graves' disease, myxedema, acromegaly** and in the majority of the cases of diabetes, lymphocytosis is found. This extremely theoretical article closes with the statement that lymphocytosis, low tolerance for carbohydrates, vasolability and high blood pressure have an endocrine origin.—J. K.

A resumé of DIABETES mellitus. Mann (R. W.), Canad. M. Ass. J., (Montreal), 1921, **11**, 243-245.

Chemical and clinical data of five cases are included. Chem. Abst., **15**, 3873.

Trauma and DIABETES. Niemeyer (H.), Geneeskundig Tijdschrift der Rijksverzekeringsbank (Amsterdam), 1921, **6**, 340-347.

Description of a man who 14 years after a severe trauma died in coma diabeticum. Nine years after the trauma the first symptoms of diabetes appeared. During these 9 years the patient always had nervous complaints. The insurance company refused to pay because it did not regard the diabetes as caused by the trauma. After a trial in which the best Dutch medical men were heard, it was, however, decided that it was highly probable that the diabetes was caused by the trauma.—J. K.

Simple method of determining the approximate degree of acidosis in DIABETES mellitus. Rabinowitch (I. M.), Canad. M. Ass. J. (Toronto), 1921, **11**, 526-528.

Details of five cases in which the Van Slyke and Palmer procedure was used. Chem. Abst. **15**, 3873

A study of the relation between syphilis and DIABETES MELLITUS. Rosenbloom (Jacob), Am. J. Syphilis (St. Louis), 1921, **5**, 634-642.

This paper contains a review of the literature and a study as to the presence of signs of syphilis in one hundred and thirty-nine cases of diabetes mellitus. Sixteen of these cases presented a positive Wassermann test, a percentage of over twelve. Eight of these cases presented signs of arteriosclerosis. It is possible that these eight cases of diabetes are syphilitic in nature, and as a part of the arteriosclerosis there would undoubtedly be present some fibrosis of the pancreas. These eight cases were subjected to intensive treatment for the syphilis, but there was no increase in their tolerance for carbohydrates. This is no doubt due to the fact that the pancreatic fibrosis still exists after the treatment. We may conclude, therefore, that in this series studied, sixteen cases presented positive Wassermann tests. In about six per cent of the cases studied the diabetes existed as a part of the syphilitic process and in about six per cent the syphilis and diabetes existed as independent conditions.

—Author's Abstract.

A study on the viscosity of the blood in DIABETES (Étude sur la viscosité sanguine chez les diabétiques). Rousseau (C.), Thèse de Paris, 1920.

The author studied the viscosity of the blood in diabetes after adding sodium citrate to it to prevent coagulation. When the viscosity was estimated the blood was centrifuged and the viscosity of the plasma was measured. The difference between these two values is considered as the viscosity of the corpuscles. In consumptive diabetes, especially when coma is coming on, the viscosity of the

total blood is largely increased. This is due to an increased viscosity of the corpuscles, the viscosity of the plasma remaining nearly constant. The viscosity has no relation to the quantity of sugar in blood or urine.—J. K.

Experimental GLYCEMIA and hyperglycemia in normal subjects (Glycémie et hyperglycémie experimentale chez les sujets normaux). Experimental HYPERGLYCEMIA in glycosurics and in DIABETICS (Hyperglycémie expérimentale chez les glycosuriques et les diabétiques). Labbé (M.), Labbé (H.) & Nepveux (F.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 397-400.

Two articles, with nothing especially new. Curves are given and the difference between hyperglycemia of normals and of diabetics are pointed out.—T. C. B.

DIABETES mellitus. Willcox (W. H.), Practitioner (Lond.), 1921, **57**, 305-321.

The author calls attention to the several types of diabetes, mentioning also the Pavy variety of alimentary glycosuria associated with arteriosclerosis and hypertension, and the so-called "diabetes innocens" in which the quantity of sugar excreted in the urine bears no relation to the amount ingested. Diabetes appears to be increasing in prevalence as evidenced in the mortality statistics of England and Wales. Willcox summarizes Allen's views on the "pancreatic amboceptor" as related to diabetes and reminds us that despite the lack of pancreatic hormone, its administration by mouth or injection has no influence in the control of diabetes. Lowering the assimilation limit for sugar or on the other hand increased carbohydrate tolerance in disease of the posterior lobe of the **pituitary** is referred to. Disturbed carbohydrate metabolism is sometimes observed in **Graves' disease,** rarely even in **myxedema.** Willcox favors the etiological importance of infections in the causation of diabetes, but has not had success in treatment with autogenous vaccines. The symptoms of hyperglycemia are recorded; also those of acidosis. Early recognition of the latter is urged in order to prevent diabetic coma from which recovery is rare. Treatment is then carefully discussed, particularly referring to the methods of Allen and Joslin.

—H. L.

Observations on the treatment of DIABETES INSIPIDUS with infundin. Bullowa (J. C. M.), Med. Rec. (N. York), 1918, **93**, 127.

This is a brief report of a case of diabetes insipidus in a boy of fifteen. When the salt intake was diminished, the amount of urine was reduced and the specific gravity of the urine increased, but it never rose above 1007. Hypodermic injections of 1 cc. of pituitrin caused a marked concentration of the urine about two and one-half to three hours after the injection. The specific gravity of

the urine usually rose to 1020, with a marked diminution in the quantity of water excreted. The subsequent fall in specific gravity was gradual. The effect of the dose, as measured by the increase in specific gravity, was about seven hours. There was no acute thirst until fourteen to sixteen hours after the administration of the pituitrin. A single dose induced, in about two minutes after its injection, marked pallor of the skin, dilatation of the pupils, and headache, accompanied by a slowing of the heart and a fall in blood pressure. The pallor of the skin lasted about fifteen minutes and the fall in blood pressure about forty-five minutes. The administration of pituitrin and of minced gland by mouth was without effect.

—J. P. S.

The results of the operative treatment of DYSMENORRHEA (Die Resultate der operativen Behandlung der Dysmenorrhoe). Forssner (H.), Upsala Läkareförenings Förhandlinger, 1921, **26**, Sept. 1, No. 5-6; Abst. Jour. Am. M. Ass. (Chicago), 1921, **77**, 1458.

Forssner admits that an unstable nervous system and tendency to emotionalism are important factors in painful menstruation. In the 153 cases of dysmenorrhea for which he was consulted during the last ten years, and for which no appreciable cause could be discovered, he found that in 88 these subjective factors were responsible for the disturbance to such a degree that by training the patient in self-control and will-power the dysmenorrhea was often practically cured. In 65 other cases he found that while this helped, yet something more was needed. The premenstrual congestion of the uterus mucosa seems to be the cause of the pains, as the uterus is too narrow, and in seeking to correct this, the uterus contracts, as with a labor pain. Among the arguments advanced to sustain this view is that the first childbirth usually puts an end to the dysmenorrhea permanently, as the uterus gets stretched. Another argument is that patients in labor with their first child have told him that the labor pains were just like those they had had in the painful menstruation. His intervention is therefore merely to stretch the uterus and cervix, aiming to induce contractions as with labor. He dilates the cervix with Hegar bougies. With young girls this cannot be done with more than a No. 10 or 12. Then he tampons the cavity of the uterus as completely as possible, and leaves it for forty-eight hours, which often induces quite painful contraction of the uterus. The tampon is then removed and a larger bougie introduced up to No. 20. He then investigates the uterus with the finger and usually follows with curetting. Then he tampons anew and leaves the tampon for another forty-eight hours. He has never had any mishaps with this technic and never infection. If the patient objects to this treatment he never tries to urge her. In 54 of the 58 cases in which he applied it, 46 per cent have never had

any dysmenorrhea since. In 34 per cent of the cases there is still a little pain at menstruation, but nothing to compare with the previous disturbances, and the women keep up and about, which was never possible before. About 20 per cent of the total say that the dysmenorrhea is the same as before or the improvement was only for a few months. The interval since has been from ten to seven years in 14 and from one to five years in others. If disturbances return it might be possible to banish them anew by repeating the procedure. The other women in his list passed through pregnancy not long after and are omitted from his figures. In conclusion he remarks that this proportion of 80 per cent cured or immeasurably improved commends this harmless method for treatment of severe dysmenorrhea. (In German).—E. N.

A case of general DYSTROPHY. (Vorstellung eines Falles von eigenartiger allgemeiner Dystrophie). Yamin, München. med. Wchnschr., 1921, **68**, 1540.

The patient was a girl of 9½ with sexual precocity, well developed **sexual organs**, good intelligence, spasms in fingers, arms, feet and legs, hypoplasia of the skin (with dirty spots), and hypoplasia of bones and muscles. The liver, spleen and lymph glands were much enlarged; the heart, **thyroid** and **hypophysis** (by radioscopy) also. Perhaps the clinical diagnosis should be: **pineal** tumor.—J. K.

The influence of ENDOCRINE preparations on gaseous metabolism (Die Wirkung der aus endokrinen Drüsen hergestellten Präparate auf den Gaswechsel). Arnoldi (W.) & Leschke (E.), Ztschr. f. klin Med. (Berlin), 1921, **92**, 364-375.

The authors studied the influence of **thymin, hypophysis** (pars anterior and posterior), **thyreoidin, adrenalin,** and **luteoglandol** on gaseous metabolism. The influence was found to be not constant even in the individual subject. When a large dose of one of these substances is given carbohydrate metabolism is first increased, but the fat and protein metabolism is also raised.—J. K.

ENDOCRINE functions and the digestive apparatus. Barker (L. F.), Med. & Surg. (St. Louis), 1918, **2**, 655-678.

An extensive critical analysis and classification of the role of the endocrine organs in digestive functions. From the summary the conclusions can be made that the outstanding features of such relations are: the diarrhea and accelerated metabolism in Graves' disease; the constipation and retarded metabolism of **myxedema**; the enamel defects and disturbances of calcium excretion in **parathyroid** insufficiency and the relation of gastric and duodenal dilatation to tetany; the large medial incisors and long intestine in status **thymo-lymphaticus**; the relation of the anterior lobe of the **hy-**

pophysis to obesity and splanchnomegaly and of the pars intermedia to diabetes insipidus and its accompanying thirst; the relation of the pancreas and the chromaffin system to the mobilization of glucose, and the hormonic significance of secretin, gastrin and anti-thrombin produced within the digestive tract.—F. S. H.

The role of the ENDOCRINES in common medical diseases. Blumgarten (A. S.), Med. Clin. of N. Am. (Phila.), 1921, 4, 1437-1507.

The author presents numerous cases showing endocrine manifestations in common medical diseases. The evidence is based on clinical data, basal metabolism tests and all other necessary laboratory examinations. The role of the thyroid and adrenal apparatus in gastric neuroses is first considered. Endocrine syndromes fall in the following categories: (1) Frank endocrine syndromes; (2) Forme fruste types of classical syndromes occurring in two forms—either a mild type or as a type with dominant symptoms in other viscera; (3) Classical manifestations of immune reaction in infections, or as the initial onset of the infection; (4) Endocrine disturbances in functional diseases as a result of disturbance in the endocrine regulating mechanism.

Gastric neuroses include: (a) Cases showing marked or slight evidence of hyperthyroidism or thyroid deficiency; (b) Cases with gastric symptoms as the earliest manifestation of hyperthyroidism and thyroid deficiency which only later manifest themselves; (c) Cases showing a domination of the thyroid or the adrenal glands in the physiology of the patient—the so-called "thyrotropes" and "adrenotropes." The author treats functional gastric neuroses as he would an underlying endocrine disturbance. Hyperthyroidism is treated by physical and mental rest, and the usual remedies for this condition. He has used adrenal cortex, however, for an underlying adrenal cortical insufficiency, on the basis of clinical data, for the relief of the hyperthyroidism, with excellent results in the improvement of the gastric symptoms and the hyperthyroidism. (This is the first report of the use of adrenal cortex in hyperthyroidism.)

The following cases are presented. The underlying thyroid disturbance is established on the clinical data of the basal metabolism determinations: (1) A case beginning with gastric symptoms after influenza, developing frank exophthalmic goitre a year later. (2) Hyperthyroidism beginning with gastric symptoms after the emotional shock of a hold up, and developing frank hyperthyroidism symptoms months later. (3) Hyperthyroidism beginning with gastric symptoms, diagnosed as an ulcer and operated upon but with no ulcer found; a year later frank hyperthyroidism developed. (4) A case of forme fruste type of thyroid deficiency. (5) Three cases of functional gastric neuroses occurring in a thyroid-dominant type of patient. (6) Functional gastric symptoms in a male patient

of the dominant adrenal type. In these cases the existing gastroptosis is a constitutional stigma, not the cause of the symptoms.

The relation of the pituitary to adolescent epilepsy and nocturnal enuresis is then considered. A few points are emphasized. The small contracted pelvis is a pituitary manifestation. Undescended testes occur in pituitary deficiency, indicating deficient gonadal development in association with pituitary deficiency. The frequency of nocturnal enuresis and fits occurring in adolescence in association with other frank pituitary manifestations, or with a forme fruste type is pointed out. Three cases are presented: (1) Acromegaly with subsequent Fröhlich manifestations and genital atrophy, occurring in adult life, with erosion of the sella turcica; (2) A case of classical Fröhlich syndrome with epileptic fits; (3) Three brothers with hereditary dyspituitarism, with marked genital atrophy, the mother of whom showed similar symptoms of dyspituitarism.—Author's abst. (abbreviated.)

On the diagnostic and therapeutic importance of the ENDOCRINE ORGANS in the pathology of the stomach (Ueber die diagnostische und therapeutische Bedeutung der Blutdrüsen für die Magenpathologie). Boenheim (F.), Deutsche. med. Wchnschr. (Berlin), 1921, **47**, 1256.

The excretion of chlorine takes place as well through the kidneys as through the stomach. In diseases of the stomach this excretion may be just as well disturbed as in diseases of the kidney. The **thyroid** mobilizes chlorine. The exophthalmos, wide pupils, increased perspiration, nervous irritability and other symptoms of Graves' disease are also found in tuberculosis and in diseases with hyperacidity of the stomach, such as ulcus ventriculi. This is, of course, not a proof that this condition is due to an abnormal function of the thyroid. It is, however, a fact that after injections of thyroid extracts the acidity of the stomach is raised. **Pancreas, hypophysis** and **gonads** seem to have the same effect on the stomach, though much less is known about them. The **pineal** seems to have no influence. The **thymus** and the **adrenals** have an opposite influence. The thymus hormone, if there is such, has a most splendid influence in many cases of hyperacidity. It diminishes the amount of chlorine in the blood and the secretion of the stomach and is specially indicated in cases with symptoms of hyperthyroidism. The same may be said for the adrenals.—J. K.

Skin diseases and the ENDOCRINE ORGANS (Ueber Zusammenhang von Dermatosen und innerer Sekretion). Brock (W.), Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1420-1421.

The author states that there exist relations between the thymus and the cutaneous epithelium. He obtained splendid results in

psoriasis, lichen ruber planus and verrucosis and ichthyosis with exposure of the thymus to x-rays. He thinks that injections of preparations of thymus probably have the same effect, though he has not hitherto had much experience with this treatment.—J. K.

(ENDOCRINE ORGANS) Studies on ENDOCRINE facies (Estudio da facies em endocrinologia). Diaz (A.), Revista dos Cursos (Porto Alegre), 1921, **7**, 214-235.

This is a clinical study illustrated with numerous photographs. It deals with the different varieties of facial expression and treats of their importance in the diagnosis of endocrine disturbances. —B. A. H.

(ENDOCRINE ORGANS) A remarkable disease: cachexia and pluriglandular insufficience of the glands with external and internal secretion (Über ein eigenartiges Krankheitsbild: Kachexie und polyglanduläre Insuffizienz der Drüsen mit äuszerer und innerer Sekretion). Edelmann (A.) & Saxl (G.), Wiener Arch. f. inn Med., 1922, **3**, 227-234.

Three interesting cases are described: (1) A woman of 52 had glaucoma, atrophy of the tongue and acidity of the stomach, fatty stools, no polyuria, no bradycardia, and defective intelligence as seen in myxedema. At autopsy there were found atrophy of all organs, but especially of the **thyroid, pancreas** and **adrenals,** together with osteoporosis. (2) A woman of 51 showed loss of hair, stupidity as in myxedema, sclerodermia, atrophy of the tongue, fat-stools and anacidity. At autopsy atrophy of all organs but especially of the **thyroid** and **pancreas,** with osteoporosis was found. (3) A man of 51 showed edema of the legs, fatty stools, loss of hair, atrophy of the tongue and anacidity of the stomach. Post-mortem there were found marked atrophy of the thyroid and slight atrophy of the pancreas and testicles, but no osteoporosis. Pulmonary tuberculosis was also noted. The authors believe that this association of manifestations constitute a disease entity and that it is caused only by severe injuries as starvation, infection, etc. It is perhaps possible that the normal functions of the glands with external secretion depend upon normal hormone production.—J. K.

(ENDOCRINE ORGANS) The colloids of the body fluids (Kolloidzustand der Körperflüszigkeiten). Ellinger (A.), Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1479.

The viscosity of the serum is decreased by administration of caffein, theobromin, strophantin, **adrenalin;** it is increased by histamin, **thymus,** extract of **hypophysis.** Extracts of **ovary** or **testicles,** and morphine and atropine have no influence.—J. K.

(ENDOCRINOLOGY) On organotherapy (Ueber Hormontherapie). Furth (O.), Wien. klin. Wchnschr., 1921, **34**, 521-522.

A very short review of the indications for organotherapy with **thyroid, hypophysis, adrenalin, thymus** and **gonads.** Nothing new. —J. K.

The ENDOCRINE ORGANS and gynecology (Innersekretorische Frage in der Gynaekologie). Halban (J.), München. med. Wchnschr., 1921, **68**, 1314-1317.

A good general review, without new facts.—J. K.

(ENDOCRINE ORGANS) Glandular dystrophies, particularly the mono-symptomatic dystrophies (Dystrophies glandulaires et particulièrement dystrophies mono-symptomatiques). Hutinel (V.) & Maillet (M.), Ann. Méd. (Paris), 1921, **10**, 198-227.

"It is difficult to classify the endocrine dystrophies on both a rational and clinical basis." However, the authors divide the mono-symptomatic dystrophies into two groups. Into the first are placed the aplasias or arrests of development, and the atrophic regressions. In the second group are placed those disturbances of abnormal nutrition from which result a modification of the character, resistance, form and functional value of the organ in question. It is impossible to give an adequate abstract of this very complete article in which with some detail there is given the role of the various endocrine glands in the production of the symptoms by which the above classification is arrived at.—F. S. H.

ENDOCRINE influence, mental and physical, in women. King (J. E.), Am. J. Obst. & Gyn. (St. Louis), 1921, **1**, 341-349.

A discussion, along philosophical and largely hypothetical lines, of the influence of the endocrine glands upon women, especially as to various phases of her psychology. The concluding line is, "Woman, with all thy glands, we love thee still."—E. N.

(ENDOCRINE GLANDS) Report of the anatomical findings in a case of pluriglandular disease [Beitrag zur Kenntnis der anatomischen Befunde bei polyglandulärer Erkrankung (Insuffisance pluriglandulaire)]. Landsteiner (K.) & Edelmann (A.), Frankfurt. Ztschr. f. Path. (Wiesb.), 1920, **24**, 339-353.

The authors report a case and briefly review the literature. The major clinical features were as follows: Female, aged 17 years, of low-grade intelligence, well nourished, dry skin, jaundice, marked development of the mammary glands, absence of axillary and pubic hair, lymphocytosis 45%, Wassermann negative, moderate secondary anaemia, died in coma. At necropsy the **pituitary** measured 15x7 mm. The **thyroid** was small, stroma increased, with definite atrophy

of the follicles. There were enlarged tuberculous bronchial lymph glands; terminal streptococcic peritonitis; high grade cirrhosis of liver with enlarged spleen. **Thymus** present, moderately fatty. Right **ovary** measured 4x1 cm. and the left 3x1.5 cm. Bony skeleton, everywhere fragile, thinned out, spontaneous fractures of the long bones. The **parathyroids, suprarenals, pituitary** and **pineal** glands are described as normal.—D. M.

(ENDOCRINE GLANDS) The growth of tissues in the test-tube under experimentally varied conditions with special reference to mitotic cell proliferation. Loeb (L.), & Fleisher (M. S.), J. Med. Research (Boston), 1919, **40**, 509-550.

The purpose of this paper is to report experiments in which the authors analyze the factors which determine the mitotic proliferation in tissues growing in culture media under experimentally varied conditions. In most of the experiments kidney tissue was used. A limited number of experiments were made with **thyroid** and **parathyroid** glands, **testicle** and **ovary.** The parenchyma and stroma of the peripheral parts of thyroid and testicle may survive transplantation into coagulum in a test tube. In both thyroid and testicle the central parts of the transplants became necrotic. The colloid of the acini of the thyroid frequently disappeared in the same way as after transplantation in vivo. The typical thyroid structure was maintained, and the thyroid cells sometimes showed mitoses. In the testicle only scattered nuclear figures, different from the typical mitoses in other organs, were observed. In the tubules the production of spermatozoa was not seen to continue in vitro. While in the thyroid in the test tube the stroma perished to a great extent even in the peripheral parts, in the testicle, on the contrary, the stroma seemed to be more resistant; this is probably due to the tendency of the testicular stroma to become transformed into interstitial cells. Passing oxygen through the container caused increase in the size of the preserved area in the pieces of thyroid, but not in pieces of the testicle. The peripheral parts of parathyroid may likewise survive in the test tube. In the case of the ovary the same kind of structures survive after transplantation into the test tube as after transplantation into subcutaneous tissue, namely, the small follicles, germ epithelium and tunica albuginea. Mitotic activity was noted in the germ epithelium, but not in the follicles, in the test tube.—J. P. S.

The ENDOCRINE origin of muscular dystrophy. Manney (N. W.), Goodhart (S. P.), & Clark (L. P.), Med. Rec. (N. Y.), 1918, **93**, 128.

Brief abstract of an article which appeared later in Arch. Int. Med., 1918, **21**, 188-215.—H. L.

(ENDOCRINE ORGANS) Anatomical and clinical study of a case of Erb-Goldflam's myasthenia gravis (Étude anatomo-clinique d'un cas grave de myasthénie de Erb-Goldflam). Marie (P.), Bouttier (H.) & Bertrand (I.), Ann. Méd. (Paris), 1921, **10**, 173-184.

Plates showing disturbances of **adrenals, thyroid** and **thymus** in this disorder.—F. S. H.

(ENDOCRINE ORGANS) Asthenias due to pluriglandular disorders of syphilitic origin. Merklen, Devaux & Desmouliere, Presse méd. (Paris), 1921, **29**, 14; Abst. Am. J. Syphilis (St. Louis), 1921, **5**, 687-688.

The manifestations of syphilis are not necessarily objective and may comprise purely subjective states such as asthenia. This knowledge is naturally due to serodiagnosis. Women are especially apt to complain of an unmotivated sense of prostration, which may be continuous or intermittent and vary more or less in degree. Ordinary therapeutic resources are used in vain. The condition passes for one of nervous invalidism. The usual resources such as visiting or change of residence brings about only a transitory amelioration, and a crisis may occur in the midst of such a change. The authors do not claim to have first discovered this morbid state for it has been described as syphilitic neurasthenia. But the latter when secondary to another process is practically an organic affection. To what system then shall we attribute it? In the present state of our knowledge we are apt to think of the endocrine glands and especially the **adrenals.** Congenital syphilis, as shown by Hutinel, may act destructively on these bodies and set up dystrophies, hence in the acquired syphilis of the adult, something of the same nature may occur. Asthenia attends on various clinical expressions of secondary syphilis, but we are not interested in the asthenia which accompanies outspoken lesions but solely in this connection in a form which appears rather suddenly during the evolution of the disease and indicates that the virus has done some damage to one or more of the endocrine glands. The blood gives a slightly positive Wassermann reaction. Specific treatment ameliorates and if persisted in may cure.—R. G. H.

(ENDOCRINE ORGANS) Salt excretion in relation to constitution (Versuche über Kochsalzausscheidung von konstitutionellen Gesichtspunkten ausbetrachtet). Moewes (C.), Ztschr. f. klin. Med. (Berlin), 1921, **92**, 376-380.

The author examined the excretion of NaCl, after administration of extra quantities in several persons. Amongst ten patients with a normal excretion, three had a **habitus asthenicus,** six **hyperthyroidism,** and one **hypothyroidism.** Of nine patients with an in-

creased excretion, four had a habitus asthenicus, three hyperthyroidism, two hypothyroidism. Of 12 patients with a defective excretion of NaCl, two showed a habitus asthenicus, seven hyperthyroidism, and three hypothyroidism. There is no relation between constitution and excretion of NaCl.—J. K.

(ENDOCRINE GLANDS) Studies on compensatory and correlated hypertrophy (Untersuchungen über kompensatorische und korrelative Hypertrophie). Nigst (P.), Schweiz. med. Wchnschr., 1921, **51**, 155-156.

Two types of work hypertrophy are distinguished: (1) compensatory, as for example, the hypertrophy of the remaining portion of the **thyroid** after the removal of three-fourths, and (2) what he calls correlated hypertrophy, as for example, the hypertrophy of the **hypophysis** after thyroidectomy. While much is known of hypertrophy in general, we are still poorly informed concerning many of the finer mechanisms involved. One of these, the influence of the nervous system, is the subject of the present report in which the kidney was studied. Two groups of rabbits were used. In one, one kidney alone was removed. In the other, after removing one kidney, all nerves going to the kidney were destroyed by dissecting the renal artery and vein and ureter as free from nerves as possible, then applying pure carbolic acid followed by alcohol to destroy any remaining fibers. The compensatory hypertrophy was as rapid and as marked in the denervated kidney as when the nerves were left intact. As an example of the so-called correlated hypertrophy, advantage was taken of the **suprarenal—thymus** interrelation. According to Matti, the suprarenals enlarge following thyroidectomy in dogs. The author thymectomized rabbits with and without denervating (cutting the splanchnic) one suprarenal. He noted no difference in the suprarenal reaction depending on denervation and concludes that neither compensatory nor the so-called correlated hypertrophy are dependent upon nerve influences.—D. M.

(ENDOCRINE ORGANS) Certain pluriglandular anomalous functions associated with psychopathic sexual interests. O'Malley (M.), J. Nerv. & Ment. Dis. (N. Y.), 1918, **48**, 1-35.

These interesting studies accompanied as they are by many photographs are suggestive but too diffuse to be conclusive, although the author does state that there is no definite mental reaction type associated with the endocrinopathies.—F. S. H.

(ENDOCRINE GLANDS) The influence of a lack of calcium in the food on the respiratory exchange (Untersuchungen über den Einflusz des Calciummangels in der Nahrung auf den respiratorischen Grundumsatz). Pedotti (F.), Biochem Ztschr. (Berlin), 1921, **123**, 272-283.

Rats were kept on a calcium-free diet and an attempt was made to deplete the body of calcium by potassium feeding. The determination of the respiratory exchange showed that a lowered basal metabolism resulted from the lack of calcium. No histological changes took place in the **thyroid, parathyroids** or bones.—F. S. H.

(ENDOCRINE GLANDS) The iron man and the mind. Pound (A.), The Atlantic Monthly (Boston), 1922, **129**, 179-189.

"The operating of automatic and semi-automatic machinery evolves evidence tending to show that fatigue, instead of being simply weariness from muscles stretched too much or too often, is rather a pathological condition, due to the poisoning of the system through over-secretion of the endocrine glands. Whatever the theorizing as to endocrine glands, it is probably true there is an excessive outpouring under nervous tension, when effort is prolonged beyond the normal fatigue limit. Glandular secretions, roused by an overstressed fraction of the anatomy, spread beyond that fraction to stimulate the rest of the man into heightened activity."—F. S. H.

The literature on the ENDOCRINE ORGANS in 1921 (Yaaroverzicht van de literatuur over de klieren met inwendige afscheiding). Stuurman (F. J.), Ned. Tijds. v. Geneesk. (Haarlem), 1921, **65**, 3077-3096.

A general review.—J. K.

Clinical ENDOCRINOLOGY. Timme (W.), Neurol. Bull., (N. Y.), 1921, **3**, 3-33.

This article is a lecture which embodies an interesting general exposition of some of the more important endocrine data together with the author's system of endocrine philosophy. It is not amenable to abstracting.—R. G. H.

(GONADS) The rôle of the nucleus in the epididymal secretion (Sur le rôle du noyau dans la sécrétion épididymaire). Benoit (J.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 946-948.

A histological description of the cells of the epididymus, showing the conditions during the secretion from the nuclei.

—T. C. B.

(GONADS) The over-appreciation of the puberty gland (Die Ueberschätzung der Keimdrüse). Biedl (A.), Deutsche. med. Wchnschr. (Berlin), 1921, **47**, 1247.

Biedl is not convinced of the truth of Steinach's teachings. The organism is sexual from the beginning and the question whether a male or female individual will be formed was determined in the structure of the ovum and the spermatozoön. Every endocrine

organ has an influence on the secondary sexual characters. This is especially true for the thyroid and the adrenals.—J. K.

(GONADS) Marked lipoid hyperplasia of both ADRENALS with foci of calcification in a pseudo-hermaphrodite with bilateral undescended testis and an accessory suprarenal in the right testis [Hochgrädige Lipoidhyperplasie beider Nebennieren mit herdförmigen Kalkablagerungen bei einem Fall von Hypospadiasis penisscrotalis und doppelseitigem Kryptorchismus mit unechter akzerrorischer Nebenniere am rechten Hoden (Pseudohermaphroditismus masculinis externus)]. Brutschy (P.), Frankfurter Ztschr. f. Path. (Wiesb.), 1920, **24**, 203-240.

Reports the case of a pseudo-hermaphroditic male infant, aged 17 days, with a clinical diagnosis of difficult labor, subdural hemorrhage, congenital heart defect and carbon dioxide intoxication. The post-mortem examination showed a large, active **thymus**, normal **thyroid**, enlarged spleen, adrenals markedly enlarged, measuring 3.8x2.2x1 cm. The surfaces of both suprarenals were nodular. There were two minute accessory suprarenals in the capsule of the right kidney. Uterus and vagina absent. Sex glands resemble testes and measure 8x6x4 mm. as compared with 10x8x7 mm. of the testes of a normal 47 cm. infant. On the right sex gland there was a small accessory suprarenal gland. The suprarenal enlargement was mainly cortical, which was very bright yellow in color. External genitalia were those of a normal female infant. Microscopically, no definite adrenal medulla tissue was found, the whole gland being composed of irregular large and small adenoma-like masses. In places, cholesterol spaces and giant cells were found. Testes and **hypophysis** showed no noteworthy changes. Reviews literature reports of cases: (1) with accessory suprarenals in genital malformations; (2) with suprarenal hyperplasia and accessory suprarenals in right testis in male pseudo-hermaphrodites; (3) with suprarenal hyperplasia and accessory suprarenals in female pseudo-hermaphrodites. —D. M.

(GONADS) Constitutional eunuchoidism. Eichhoff; Berl. klin. Wchnschr., 1921, **58**, 818.

The patient is a healthy man of 34, rather large but of the female type. The pelvis has the female form. There are but few hairs on the trunk or the face. The muscles are well developed. The voice is high pitched. The external genitalia are underdeveloped but potentia coeundi and sexual desire are normal. Though he has been married seven years he has had no children. A skiagram of the skull shows an extremely small sella.—J. K.

(GONADS) The scurf of rats and its relation to Steinach's rejuvenation (Ueber die Rattenäude und ihre Beziehung zu den Stein-

achschen Verjungungsversuchen). Fiebiger, (J.), Wien. klin. Wchnschr., 1921, **34**, 364-366.

Steinach's book on rejuvenation contains many splendidly executed photographs. From these Fiebiger made the diagnosis of "scurf" in Steinach's animals. Steinach himself points out that animals with lice are of no use for his experiments since they exhibit senile symptoms. Steinach does not speak about scurf, but the symptoms which he considers as senile—loss of hair on the scrotum, bald spots on the back, loss of weight, loss of sexual desire—are all symptoms of scurf. It is a well known fact that when horses are attacked by scurf they rapidly become senile. Fiebiger holds that Steinach's results are probably not due to his operations, but to his cure of the scurf by proper nursing, feeding and cleaning of the animals.—J. K.

(GONADS) Sexual neutralization obtained by means of orchilytic and ovariolytic serum (Neutralizzazione sessuale ottenuta mediante sieri orchilitici ed ovariolitici. Giuliani (R.), Ann d'ig (Roma), 1920, **30**, 323-326; Abst., Pathologica (Genova), 1921, **13**, 542-578.

The result of these experiments show how through orchilytic serum a degeneration of the testis can be obtained to the extent of hindering their very function. A microscopic examination revealed deep alteration of the parenchyma that had become granular. The seminiferous tubules could hardly be identified. Albuginea and connective tissue remained unchanged.—G. V.

(GONADS) Congenital idiocy (Angeborene Idiotie). Kellner, Berl. klin. Wchnschr., 1921, **58**, 1393; Deutsche med. Wchnschr. (Berlin), 1921, **58**, 1393; Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1511.

A boy of 10 is described with extremely small generative organs. In the penis no corpus cavernosum was present and testicles could not be detected.—J. K.

(GONADS) Youth and old age (Jugend und Altier), Kohn (A.), Wien. klin. Wchnschr., 1921, **34**, 494.

The author does not agree with Steinach's teachings. It is true that after ligation of the vasa deferentia the interstitial cells of the testis increase in number; but this is not a proof that they possess an increased endocrine function.—J. K.

(GONADS) Steinach's theory (Die Lehre Steinachs). Lipschütz, Deutsche med. Wchnschr. (Berlin), 1921 **47**, 1247.

The author is absolutely sure that the interstitial cells exert an endocrine function. He believes that the embryo is asexual and

that the development of the interstitial cells is the cause of sexual differentiation.—J. K.

(GONADS) The so-called interstitial gland implantation. To whom is the credit due? Lydston (G. F.), Am. J. Surg. (N. Y.), 1920, **34**, 77-80.

The author reviews the early attempts at transplantation of **reproductive glands,** beginning with Berthold's work on fowls in 1849; notes the first reported transplantation in this country by Hammond and Sutton in 1912; and gives in detail his own experiments and conclusions. The terms "interstitial glands" is of newspaper science origin—while the "between cells" of Leydig are supposed to secrete hormone, they are not true gland cells and transplantations are not confined to the "glands interstitielle." In 1914 the author found that part of a gland transplanted into its own tissues became in part embedded, with formation of a new circulation. This experiment was followed by successful operation upon both sexes and upon fowls. The essayist concludes that the procedure is practicable; that the material can be preserved a reasonable time prior to operation; that the hormone of the implanted gland is helpful in chronic disease, senility, defective sex-development, certain skin conditions, mild anteriosclerosis and anemia; and that it is not necessary that the implanted gland should remain permanently to secure beneficial results. The priority of Voronoff, of Paris, in the field is disputed, the author having found no scientific contributions from his pen prior to his visit to this country.

—C. R.

(GONADS) Pseudo-hermaphroditism (Pseudo-ermaprodictismo androgeno). Massari (G.), Gazz. degli Osp. (Milano), 1921, **42**, 872.

Report of a post-mortem examination. The patient gave the impression of a man with normal external sexual organs. The scrotum, however, was empty. In the abdomen near the inguinal regiona uterus was found with two bodies, resembling ovaries. They were, however, testicles with vasa deferentia.—J. K.

On the cytological localisation of a peroxydase, and on its presence in the GONAD cells (Sur les localisations cytologiques d'une peroxydase et sur sa présence dans des cellules sexuelles). Prenant (M.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 808-810.

Histological.—T. C. B.

(TESTES) Symptoms of eunuchoid feminilism and tuberculosis (Sindrome di femminilismo eunucoide ed infezione tubercolare). Sega (A.), Gazz. d. Osped. (Milano), 1921, **42**, 946-950.

Description of a man of 24 with tuberculosis of the lungs and with small testicles. After ingesting 150 gm. of glucose a slight glycosuria resulted. At autopsy the testicles were found atrophic, with only a small number of canaliculi. The connective tissue was enormously developed. There were a very few interstitial cells of polyhedrical form.—J. K.

Experimental studies on the GONADS in mammals (Études expérimentales sur les glandes sexuelles chez les mammifères). Sand (K.), J. de physiol. et de pathol. gén. (Par.), 1921, **19**, 305-322.

An abstract of the author's book published in Danish in 1918. Some of the conclusions arrived at are: Special importance is to be attached to the interstitial cells of Leydig in the testis, the theca-luteal tissue and corpus luteum in the ovary. Transplantation of testis, when successful, causes complete development of sexual characters in the male and hypertrophy of the clitoris in the female. Transplantation of the ovary into the male causes hypertrophy of the mammary glands. The ovary is able to grow in the interior of the testis, thus producing bisexual characters.—Physiol. Abst.

(GONADS) A case of dystrophic geroderma (Su un caso di geroderma distrofico). Tramontano (V.), Gazz. internaz. di med. (Napoli), 1921; abst., Pathologica (Genova), **13**, 549.

With the accentuated hypoplasia of the gonads the patient presents unusual high stature and typical disposition of fat, while the epiphyseal junctions have been considerably delayed. The limbs are unusually long and the secondary sexual characteristics are underdeveloped. No genital function, no libido. The histological examination of the testis showed an alteration of the seminal tubules, absence of the normal cells, small epithelial cells with scanty protoplasm and resting nucleus. The condition, more than hormonic, seems to be due to a fault in development of the spermogenic function of the testis with disfunction of the **thyroid** and **hypophysis.**

—G. V.

(GONADS) Proportions of the body and intersexuality as functions of internal secretion (Körperproportionen und Intersexualität als Ausdrückformen der inneren Sekretion). Weil (A.), Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1247-1248.

A short note. There seems to be a relation between the length of the body, the physical sexual signs and the psychical sexual symptoms.—J. K.

(GONADS) The measures of the body in homosexuals as a sign of a specific constitution (Die Körpermässe der Homosexuellen als Ausdrucksform ihrer spezifischen Konstitution). Weil (A.), Berl.

klin. Wchnschr., 1921, **58**, 1225, and Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1311.

The size of the extremities and the trunk depend upon the endocrine system. **Hypophysis, thyroid** and **thymus** intensify growth. The gonads, however, during puberty, prevent further growth. The author finds that in homosexuals, male as well as female, the various anatomical indices were abnormal and believes that this is probably due to the abnormal function of the gonads in homosexuality. (It is to be noted that this abnormal function has never been definitely proved.)—J. K.

Further investigations on the humoral action of the nerves of the HEART (Weitere Untersuchungen über humorale Uebertragbarkeit der Herznervenwirkungen). Loewi (O.), Klin. Wchnschr. (Berlin), 1922, **1**, 22-23.

If the heart of a toad is filled with a Ringer's solution and the vagus or accelerator nerve is stimulated and if after this the Ringer's solution is brought into a fresh heart it has the same effect on this second heart as if its vagus or accelerator were stimulated. Hence some chemical substance is liberated, perhaps a cardiac hormone. If the vagus and accelerator are stimulated together generally first a vagus and then an accelerator effect is obtained. The content of the heart has just the same action on a fresh heart. It is, however, possible by a special way of stimulating both nerves together to get only a vagus effect, but also in these cases the content of the heart first produces in a fresh heart a vagus and then an accelerator effect. —J. K.

Transitory symptoms of HYPERTHYROIDISM following tracheobronhcoscopy (Syndromes hyperthyroidiens transitoires provoqués par la trachéo-bronchosopie). Rist (E.) & Weiss (M.), Bull. et mém. soc. méd. des Hôp. d. Par., 1921, **45**, 1405-1409.

Report of two cases as described in the title. The disturbances are tentatively attributed to the traumatism of the laryngeal mucosa with consequent irritation of the cervical sympathetic connections.—F. S. H.

The morphogenesis of the HYPOPHYSIS in the tailed amphibia. Atwell (W. J.), Anat. Record (Phila.), 1921, **22**, 373-390.

The development of the pituitary body is studied in Ambystoma and comparisons of the adult morphology made for Necturus, Spelerpes and Amphiuma. It is found that the pars tuberalis, which in the Anura becomes detached at metamorphosis to form two discrete epithelial plaques, remains attached to the anterior lobe in the tailed amphibia, even in adult life.—Author's Abst.

(HYPOPHYSIS) Atypical adiposo- genital syndrome (Syndrome adiposo-genital atypique). Babonneix & Denoyelle, Bull. et mém. soc. méd. des hôp. d. Par., 1921, **45**, 1619-1623.

Case report of a man of 50 years with mammary hypertrophy, manifest obesity, large head, short neck, atrophy of the hands, cervical kyphosis, strabismus and nystagmus. Psychically he was puerile and cyclothymic. The sexual apparatus was mediocre, the testicles small. Wassermann negative. Urine and cerebro-spinal fluid normal. The x-ray showed an enlarged sella turcica.—F. S. H.

Cytological observations on the pars buccalis of the HYPOPHYSIS cerebri of man, normal and pathological. Bailey (P.), J. Med. Research (Boston), 1921, **42**, 349-381.

A cytological study of the anterior lobe or pars buccalis of the human pituitary, paying especial attention to the presence and numbers of mitochondria. In one case of active acromegaly with an eosinophilic struma the mitochondria were not increased. This does not render support to the hypersecretion theory of the origin of acromegaly. B. also describes a method for differential staining of the eosinophilic and basophilic granules and from his studies concludes that while these two types of granular cells arise from indistinguishable reserve or parent cells they never revert. The histological findings in eight cases of adenomatous enlargement of the anterior lobe are given. Cells of the basophilic type were absent in all. This well known fact is discussed without any suggestion of its possible physiological significance. In conclusion it is stated that hyperplasia of the anterior lobe in acromegaly is probably secondary to some underlying biochemical disturbance and while it is widely held that this hypertrophy is indicative of hyperfunction, there is no experimental evidence to support such a conception.

—D. M.

Clinical contribution to the HYPOPHYSEAL theory of DIABETES mellitus (Kasuistischer Beitrag zur hypophysären Theorie des Diabetes mellitus). Bleibtreu (R.), München. med. Wchnschr. 1921, **68**, 1153-1154.

A description of a case of diabetes with an enormous polyuria and a slight glycosuria with acetone or diacetic acid.

The excretion of NaCl was not the same as in diabetes insipidus. Pituglandol had no effect on diuresis. An x-ray of the skull showed the sella turcica and the proc. clinoidei apparently absent. As the Wassermann test was negative the author believes that the diagnosis is tumor of the hypophysis. Administration of thyroidin or oophorin had no effect.—J. K.

(HYPOPHYSIS) On the so-called and the true parahypophysis (Over de zoogenaamde en een ware parahypophyse). Bolk (L.),

Nederl. Tijdschr. v. Geneesk. (Haarlem), 1921, **65**, (II.) 1913-1914.

The parahypophysis or the pharyngeal hypophysis is a small endocrine organ which in man is situated against the base of the skull near the os basilare. Bolk states that it takes its origin from the chorda dorsalis. He suggests that the term "retropharyngeal body" would be preferable to parahypophysis. The structure is not found in many animals, but is regularly present in man. It is held that there is probably a relation between the existence of this body and a complicated course of the chorda dorsalis. In structure the retropharyngeal body is complicated. In addition to the part which has its origin from the chorda dorsalis, another is found which arises from the epithelium of the pharynx. A true parahypophysis, arising from the hypophysis, has been observed by Bolk in the dog only.—J. K.

Concerning malignant HYPOPHYSEAL tumors and hypophyseal cachexia (Zur Kenntnis der bösartigen Hypophysengschwülste und hypophysären Kachexie). Budde (M)., Frankfurter Ztschr. f. Path. (Weisb.), 1921 **25**, 16-34.

Reports a case of malignant pituitary tumor with metastases in a woman, aged 27 years. She was first operated on for a tumor in the left side of the neck, which on account of its relation to the carotid artery, was thought to be a carotid gland tumor. Microscopic examination at the time showed it to be a malignant epithelial tumor probably of branchiogenic origin. The patient failed rapidly and developed signs of brain tumor involving the basal region. Autopsy showed a tumor mass 2 cm. in diameter occupying the site of the pituitary gland with nodular extension down over the pons and medulla to the foramen magnum. There were also metastases in the lungs as well as a recurrence in the neck. Examination of the tumor from the several sites revealed a single type. The cells were granular. The basophilic and acidophilic cells, so characteristic of the anterior lobe of the pituitary, predominated. He points out the rarity of metastases in pituitary tumors and the peculiar clinical interest in that there were no symptoms suggesting primary pituitary disease.—D. M.

PITUITRIN-like substance in cerebrospinal fluid. Dixon (W. E.) & Cow (D.), Proc. Roy. Soc. Med. (Lond.), 1921, **14**, Sect. Ther. & Pharm., 6.

Normal cerebrospinal fluid has no pituitrin action; after injection of extracts of intestinal mucosa or ovary it appears after an hour to contain a substance with the properties of pituitrin. After injection of pituitary extract, the fluid gave the pituitrin effect im-

mediately. Extract of **testis**, epididymus, liver, **pancreas** choroid plexus, etc., histamine, pilocarpine, and **adrenaline** had no effect. —Chem. Abst., **15**, 3869.

Cutaneous alterations in toads after removal of the HYPOPHYSIS (Alterations cutanées chez les crapauds hypophysectomisés). Giusti (L.) & Houssay (B.A.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 597-598.

Three to ten days after hypophysectomy the skin takes on a deep bronze to black color, while the ventral surface becomes grayish or brown. Ulcerations appear at points of contact with the ground, and sometimes also on the snout and about the eyes. It is interesting to compare these results with those of others who have demonstrated that early destruction of the hypophysis results in albino larvae that do not metamorphose, and raises a number of questions difficult to solve.—T. C. B.

(HYPOPHYSIS) A case of acromegaly (Ein Fall von Akromegalie). Haexel (A.) München. med. Wchnschr., 1921, **68**, 1336.

Demonstration of a woman of 28, who shows typical symptoms of acromegaly and who never has menstruated. The symptoms are much more marked on the right side than on the left. No symptoms of brain pressure. The x-ray does not show a large sella, but its base is not distinct. **Thyroid** is not palpable; skin is fat, no myxedema. Hair growth and genitals normal.—J. K.

(HYPOPHYSIS) A peculiar process of the diencephalic floor in the fetal calf. Holt (E.), Anat. Rec. (Phila.), 1921, **22**, 201-205.

A median ventral downgrowth from the floor of the brain is observed in calf embryos from 40 to 310 mm. in length. The structure lies just in front of the hypophysis. The author ascribes no significance, either morphological or endocrine, to it.—W. J. A.

Absence of the pars buccalis of the HYPOPHYSIS in a 40 mm. pig. Holt (E.), Anat. Rec. (Phila.), 1921, **22**, 207-215.

Description of a 40 mm. pig embryo showing complete absence of the pars buccalis of the hypophysis. The neural lobe is well developed. The thyroid, ovaries, and adrenals were normal for this stage of development.—W. J. A.

The Histology of the human HYPOPHYSIS in kidney disease (Ueber das Strukturbild der menschlichen Hypophyse bei Nierenerkrankungen). Höppli (R.), Frankfurter Ztschr. f. Path. (Wiesb.) 1921, **26**, 22-49.

The work was suggested by Berberling's report of finding an increase in the basophilic cells of the hypophysis in cases of renal

disease. The material from the Pathological Institute at Kiel showed 45 cases with renal disease such as chronic glomerular, arteriosclerotic and parenchymatous nephritis, amyloid disease, tuberculosis and congenital cysts. Of these, 30, or 66.7% had an increase in the number of basophilic cells in the hypophysis. In 75 control cases only 24, or 32% showed an increase in basophilic cells. He confirms Berberling's observations. No suggestion is offered of the possible physiological significance of these findings.—D. M.

Action of extracts of HYPOPHYSIS on cerebral polyuria (Action des extraits d'hypophyse sur la polyurie cérébrale). Houssay (B. A.), & Hug (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 681-683.

In dogs it has been shown that the injection of extract of hypophysis is followed by an increased secretion of urine for the first two to four hours following the injection. If diuresis has been caused by the ingestion of large quantities of water, the injection of hypophysis prevents the absorption of the water, and the diuresis is sometimes diminished. The 24 hour quantity of urine varies due to a general depression of the animal; he eats less and drinks less. The authors have observed similar effects in animals suffering from polyuria caused by extirpation of the hypophysis, or by puncture of the optopeduncular region. The polyuria was augmented in all cases during the first few hours. If the polyuria was very marked, there was little effect on the 24 hours quantity, because the animal continued to urinate and to drink. If, however, the polyuria was less marked there was a diminution, due to the fact that the animals did not drink as much as usual.—T. C. B.

Secretion of the HYPOPHYSIS and of the PARATHYROID glands (Experimentelle Beiträge zur inneren Sekretion der Hypophysis cerebri und der Glandulae parathyreoideae). Izumi (G.), Mitt. a. d. Hyg.-Inst. u. d. Path.-Anat. Inst. (Zurich), 1920, 37 p.

In order to know the function of the endocrinous glands, especially of the pituitary and parathyroid, the author studied the reciprocal relations between the pituitary and parathyroid, the pituitary and **thyroid,** the thyroid and parathyroid, and the pituitary and **gonads,** using 49 cats and 127 rats. Some of them were castrated and from the others the thyroids or parathyroids were removed totally or partially by a careful operation. After clinical observation during two, five and ten months, they were killed by ether narcosis to study the histology of the above mentioned glands. The parathyroidectomized rats and cats showed that the chromaphile cells, especially basophils, decline remarkably in number and size in the pars anterior of the pituitary; while the chromophobe cells, especially transition and mother-cells increase in number. After the removal of the parathyroid, the pituitary body of the rat in almost every case became smaller, while on the contrary, that of the cat

always enlarged from two to four times the normal size. The source of this enlargement is mainly the proliferation of the cellular element of the pars intermedia. In the thyroidectomized cats the pituitary was always enlarged, due principally to proliferation of the pars anterior, but partially to hypertrophy of the lobulus pedunculars. The source of the former is the extreme proliferation of large granulated basophilic cells, and a few of the eosinophilic cells; while the latter has an increase of the epithelial cells, which accumulate much of the secretion in its acinus. According to the author's experiments, enlargement of pars intermedia cannot be demonstrated in thyroidectomized cats, but only in parathyroidectomized. The pituitary of castrated rats was larger than normal and this is due clearly to the appearance of the "castratcells" in pars anterior. Tinctorial reactions indicate that these cells are derived from the eosinophilic cells of pituitary. At the late period of the experiments an increase of the eosinophilic cells in pars anterior also was noted. Feeding the parathyroidectomized rats with phosphorus-cod-liver-oil and calcium lactate had no favorable influence on the opaque degeneration of the teeth that occurred. Total or partial removal of the thyroid or total castration had no clinical effect upon the course of tetany, which is seen after enucleation of the parathyroids of the rat.—Author's Abst.

Cysts of the HYPOPHYSIS. Kanavel (A. B.), with pathological report by Jackson (H.), Surg., Gynec. & Obst. (Chicago), 1918, **26**, 61-70.

Kanavel reports three cases of typical Fröhlich's type of hypophyseal disease. All of these patients were operated upon by a technique described by the author. In each instance there was a cyst in the region of the hypophysis. One of the specimens was carefully studied by Jackson, who found it to be typical of the cysts described by Erdheim as originating from remains of the craniopharyngeal duct. These tumors, which are usually cystic, closely resemble adamantinomas. The wall of the cyst here described showed masses of stratified epithelium sharply demarcated from the connective tissue stroma by a layer of tall cylindrical cells resembling the basal cell layer of a mucous membrane. Between this basal layer and the cavity of the cyst there were several strata of flattened cells with intercellular bridges like the prickle cells of the stratum spinosum. Here and there were areas of epithelial cells undergoing hydropic degeneration with the formation of small pseudocysts. No cells of the pituitary body were found in the sections. The article is well illustrated.—J. P. S.

(HYPOPHYSIS) Pituitrin in obstetrics (Nog eens mijn standpunt tegenover het gebruik van pituitrine in de verloskunde). Kouwer (B. J.), Vox medicorum (Utrecht), 1921, **21**, 185-186.

Warning against careless use of pituitrin without strict indications.—J. K.

(HYPOPHYSIS) A case of dwarfism (Ein Fall von Zwergwuchs). Maas (O.), Berl. klin. Wchnschr., 1921, **58**, 681.

The patient was 32 years old and 123 cm. tall. During the preceding three years he had become very stout. He had no hair in the axillae and poorly developed pubic hair; the **testicles** were normal and the penis large. The skiagram showed changes in the sella turcica. There was no **goiter.** Intelligence was good. **Metabolism** was low. The diagnosis was hypophyseal dwarfism.—J. K.

(HYPOPHYSIS) A simple method of obtaining premature eggs from birds. Riddle (O.), Science, 1921, **n.s. 54**, 664-666.

Eggs of various stages of immaturity are obtained without killing the bird, by the injection of .022 cc. "Pituitrin" in the Ringdove. Injections are best made intramuscularly. Eggs are laid, usually from 6½ to 25 minutes following the injection. They were laid at stages of immaturity varying from 4 to 26 hours.

—F. A. H.

The therapeutic uses of the anterior PITUITARY gland. Scott (T. B.) & Broderick (F. W.), Practitioner (London), 1921, **107**, 278-287.

The authors point out that there has been widespread use of the posterior lobe extract, but comparatively little clinical use in England of "Pitglandin," the "active principle" of the anterior lobe. The influence of this portion of the pituitary on growth and sexual development is then referred to and attention is called briefly to gigantism and acromegaly, as respectively preadolescent and postadolescent hyperpituitarism, and to the pre- and post-adolescent deficiency syndromes. Anterior lobe therapy is recommended for rudimentary development of **uterus** and **ovaries** with scanty menstruation or amenorrhoea; also for enuresis; for some cases of epilepsy; and combined with **thyroid** for premature senility. From the fact that the anterior pituitary influences bone growth, its extract is advised in dental caries and to help calcify the teeth, especially when combined with **parathyroid** and **suprarenal.** This combination was fed to a rabbit and at the end of two months the incisors of the "plurigland rabbit" were perceptibly longer than those of the control from the same litter. These teeth were analysed for the total amount of inorganic matter and the total calcium content. The authors give the impression that anterior pituitary extract (oral administration) is beneficial in many conditions, but little proof is submitted.—H. L.

Experimental criticism of the biological dosage of the hypertonic principle of the HYPOPHYSIS (Critique expérimentale du dosage biologique du principe hypertonisant de l'hypophyse). Stern (L.), & Peyrot (R.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 804-806.

Trendelenburg and Borgmann claim to have determined quantatively the efficacy of hypophysis extract by comparing its action with that of histamine on the uterine horn of the guinea pig. Their results contradict some observations of the authors and they have gone over the matter again, by establishing the minimum quantity necessary to produce augmentation of tonus in smooth muscle. Their tabulated results show such variations from experiment to experiment, that they conclude there is no constant agreement between the action of histamine and various preparations of hypophysis, and that the content of active principle cannot be determined by this procedure.—T. C. B.

(HYPOPHYSIS) An investigation of some of the factors which may determine the keeping qualities of infundibular extract. Tate (G.), Pharm. J. (Lond.), 1921, **106**, 486-505.

The extract, exposed to direct Hg-vapor light for 1 hr. at 8-in. distance, deteriorated only about 5%; in white or amber glass ampoules it retained its activity. As to the effect of heat and acidity, the results of Adams, Fenger and Hull, and Abel and Nagayama are quoted. Tate found no decrease of activity in a certain extract after boiling for 30 minutes (the extract being "thermostable"); nor upon exposure of the same extract to 38 degrees for 25 days after addition of 0.2 to 2% AcOH in 5 samples. Tate thought a thermostable extract might be serviceable after storing in a tropical climate, e. g., in India, but parallel experiments on samples of the same origin and the same acidity did not bear out this assumption. Keeping such drugs at a temperature not above 80 degrees F. will probably best prevent excessive deterioration. In discussion, the claim of permanency of these extracts on boiling is doubted. The methods of physiological testing need re-investigation.

—Chem. Abst. **15**, 3895.

(HYPOPHYSIS) Experimental gigantism produced by feeding pituitary gland. Uhlenhuth (E.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **18**, 11-14.

By feeding anterior lobe of pituitary several Amblystomae have been made to grow materially beyond normal size. The experiments were controlled both by keeping certain animals under the same conditions as the pituitary fed and by comparing the "giants" with the largest specimens found in museums. Anterior lobe feeding produced accelerated growth only in the post-larval stage.

Posterior lobe feeding retarded growth. The magnitude of overgrowth is indicated in the proportion between the lengths of one experimental and one control animal, namely 264: 192 mm.

—R. G. H.

Tumor of the HYPOPHYSIS. Wechsler (I. S.), Neurol. Bull., N. Y., 1918, **1**, 331-334.

A clinical report of a male white patient, aged 45 years, the major clinical symptoms being blindness, severe constant frontal headaches, without signs of acromegaly or of Fröhlich's syndrome, but x-ray examination showed an enlarged and eroded sella turcica. The differential clinical diagnosis was tumor of the pituitary.—D. M.

Psychical disturbances in diseases of HYPOPHYSIS (Psychische Störungen bei hypophysärer Fettsucht). Weygandt (W.), München. med. Wchnschr., 1921, **68**, 1356-1357.

The following cases are reported:

1. A girl who had regular menstruation when she was 15, stopped when she was 16½. When she was 17½ she grew fat and menstruation returned. Abderhalden's reaction was positive. An x-ray examination showed an enlarged sella turcica. She died when she was 22½. At post-mortem a gliosarcoma of the base of the brain was found. During her disease she was always extremely bright.

2. A boy of 15, was already very fat; at 13 months the x-ray examination was positive. Psychically he was an idiot with a very vivid temper. The penis was very small; the scrotum did not contain testicles.

3. A boy of 19 with dystrophia adiposo-genitalis. He is very cheerful, and inclined to caress any person he sees. He is restless.

4. A boy of 17 with dystrophia adiposo-genitalis. Abderhalden's reaction with hypophysis positive. He is always cheerful, talks nonsense. The administration of pluriglandular extracts resulted in improvement.

5. A woman of 32 with adiposity. Sella turcica normal. Abderhalden's reaction with **thyroid** positive, with hypophysis negative. Her psychical development is that of a child of 5. Her greatest pleasure is to play with a doll (according to the description this was not a case of dystrophia adiposo-genitalis.)

From these and other cases it is concluded that in diseases of the hypophysis, whether they are caused by tumor, by hydrocephalus or by another pathological process there exist psychical symptoms. Imbecility and idiocy is frequently met with. The temperament is generally cheerful with a special inclination to wit and jesting.—J. K.

Cytological notes relative to the HYPOPHYSIS (Notes cytologiques relatives a l'hypophyse). Winiwarter (H. de), Compt. rend. Soc. de biol (Paris), 1921, **85**, 871-874.

Histological.—T. C. B.

(HYPOPHYSIS) Retarted eunuchoidism caused by syphilis (Spät-eunuchoidismus auf syphilitischer Basis). Wittgenstein (A.) & Kroner (K.), Berl. klin. Wchnschr., 1921, **58**, 1185-1186.

A man of 47 was apparently normal till he was 43, then he showed symptoms of weariness and a positive Wassermann test. His aorta was large, as was shown by x-ray examination. He had the look of an old man, a dry skin. Psychically he was depressed; his sexual desires had disappeared. The diagnosis dementia paralytica was made. His voice became gradually high pitched and he was drowsy. His hair was brittle, he was very fat, he had nearly completely lost his beard, his pubic and axillary hair. The penis was small, the testicles atrophic. The sugar tolerance was higher than normal. There was polyuria. The authors believe that the disorder is caused by syphilitic disease of the posterior lobe, although the skiagram of this region was negative.—J. K.

A brief experimental study of the morphology of the heart muscle following HYPOTHYROIDISM. Brooks (H.) & Larkin (J.), Am. J. Med. Sci. (Phila.), 1918, **155**, 66-70.

Rabbits were thyroidectomized and the hearts removed and examined from 2 days to 6 weeks after the operation. No morphological changes in heart musculature were found.—F. S. H.

INFANTILISM and DWARFISM (Zur Kenntniss des Infantilismus und Zwergwuchses). Brandis (G.), Deutsches Arch. f. klin. Med. (Leipz.), 1921, **136**, 323-346.

A careful report of three cases with a good review of the pathogenesis of infantilism. One case of infantilism in a woman of 27, is of interest because of the fact that the sella appeared normal, bone development was retarded, there was no alimentary or adrenalin glycosuria, and treatment with pituitary and ovary gave no results.
—J. K.

The nature of innervation and its relations to the INTERNAL SECRETION (Über das Wesen der Innervation und die Beziehungen zur Inkretbildung). Abderhalden (E.), Klin. Wchnschr. (Berlin), 1922, **1**, 7-8.

It is not yet known precisely how the nerves act upon the organs which are innervated by them. It is possible that in the stimulated nerve a substance is formed which acts upon the muscle

or on the glands. The author gives a review of the newer literature bearing on this subject.—J. K.

The importance of the INTERNAL SECRETIONS in diseases of the skin especially in psoriasis (Die Bedeutung der inneren Sekretion bei Hautkrankheiten, speziell bei Psoriasis). Weinhardt. München. med. Wchnschr., 1921, **68**, 1405.

The author believes that psoriasis is an endocrine disturbance. In a number of cases x-ray treatment of the **thymus** was followed by cure or at least by a very marked improvement.—J. K.

INTERSTITIAL cells PLACENTA toxin and eclampsia (Ueber interstitielle Zellen Placentatoxin und Eklampsie). Fellner (O. O.), Zentralbl f. Gyn. (Leipzig), 1921, **45**, 1435-1441.

The author described a "feminin Sexuallipoid." He found it in **corpus luteum, placenta** interstitial cells of **ovary** and **testicle.** This substance contains a toxic material which is volatile, soluble in alcohol, ether and acetone, and probably is an amine of a lipoid. Subcutaneous injection of this substance in animals produces spasms and in larger doses death. It is, however, not probable that it has anything to do with the pathogenesis of eclampsia.—J. K.

Studies on the conditions of activity in endocrine glands. VIII. Some effects on the denervated heart of stimulating the nerves of the LIVER. Cannon (W. B.) & Uridil (J. E.), Am. J. Physiol. (Balt.), 1921, **58**, 353-364.

After removal of the adrenals stimulation of the splanchnic causes a faster rate of the denervated heart. Stewart and Rogoff attribute this to rise of pressure, increased mobilization of sugar, etc. The authors have investigated this phenomenon, and found that it occurs when the vena cava is closed just below the liver; also when the portal vein is closed. If the hepatic artery and portal vein are closed the effect is greatly reduced or abolished. Massage of the liver will itself induce a faster heart rate. Section of the hepatic nerves shows no increase of the heart beat, or an increase of only 2 beats per minute. Stimulation of the hepatic nerves causes more or less increase of heart rate. The inference is drawn that some agent arising in the liver is the occasion of the faster beat. This can account for the discrepancies in Cannon's and in Stewart and Rogoff's results.—T. C. B.

The terminal phenomena after MENOPAUSE induced by x-rays (Die Aufsfallserscheinungen nach der Röntgenmenopause). Fuchs (H.), Strahlentherapie (Berl. u. Wien.), 1921, **12**, 742.

On the basis of 69 cases the author compares the terminal condition of women in whom an artificial menopause has been pro-

duced according as that condition has followed an x-radiation, ovariectomy, or hysterectomy. The paper is entirely clinical and goes into some detail. He claims that under x-rays psychical equilibrium is better preserved, vasomotor changes are fewer, and there is less disturbances of the entire generative system.—Med. Sci. **5**, 284.

MENSTRUATION and OVULATION. Frankl (O.), Dublin J. M. Sc., 1921, **4**, 481-491.

An excellent review of the present status of our knowledge of the subject. It embraces a discussion of the relation of various endocrine glands to the genital organs.—E. N.

Experimental study of the physiology of MENSTRUATION (Contribución experimental para el estudio de la fiseologiá de la menstruación). Ramirez (E.), Rev. Mex. de Biol. (Mexico), 1921 **2**, 24-33.

Menstruation is intimately connected with the function of the ovaries. No corpora lutea are found at the beginning of either menstruation or rutting, hence they are not the determining cause of menstruation. On the other hand, the chondrioma of the small interstitial cells of the ovary in animals in rut are formed with enormous activity. Lipoid substances are also produced. During rutting the modifications of the uterus are wholly comparable to those during menstruation. The secretion of the interstitial tissue produces the catemenial symptoms and is probably eliminated in the flow, which contains a great quantity of lipoids distinct from cholesterin. When the uterus is lacking and the ovaries persist, true phenomena of intoxication and vicarious hemorrhages appear. Histologic study of the uterus during menstruation and cytological study of the menstrual detritus from the cervical canal show that a substance of ovarian origin produces uterine cytolysis. The ovarian hormones may be clearly demonstrated by the Abderhalden reaction, allowing the sanguineous serum to act on the uterine mucosa; except during menstruation the reaction is negative. Uterine mucosa can advantageously be used as substrate in the Abderhalden pregnancy test.—Author's abst. (abbreviated).

Influence of MENSTRUATION on the food tolerance in DIABETES mellitus. Rosenbloom (J.), J. Am. M. Ass. (Chicago), 1921, **76**, 1742.

This paper contains studies on 2 cases of diabetes mellitus in which the patients lost all their food tolerance with the onset of their menstrual period. Two tables are presented, showing that when the patients were put on starvation diets, the glycosuria that previously developed during menstruation did not reappear. One of the patients later, during her menstrual period, developed an acute

acidosis and died. During this period she was on a diet that had previously kept her sugar-free and free from acidosis. The author believes that the explanation of the loss of food tolerance in the 2 cases described is some temporary alteration in the function of the gonads, either an increased secretion or a lack of correlation with other of the endocrine organs.—E. N.

A study of the hemoglobin after childbirth with special reference to the resumption of MENSTRUATION. Rucker (M. P.), Am. J. Obst. & Gyn. (St. Louis), 1921 **1**, 964-972.

From a study of 74 cases, Rucker reaches the conclusion that hemoglobin is a deciding factor in the post-partum resumption of menstruation. Immediately after delivery there is a definite drop in the hemoglobin, from which the patient slowly recovers. The average parturient begins menstruating when the hemoglobin reaches about 75 per cent. Certain subjects menstruate with a much lower hemoglobin, and there are patients who have had some anemia for a long time. Retrodisplacement with its pelvic hyperemia is also a factor in the early restoration of the menstrual phenomenon.
—E. N.

Diseased condition of bones and joints as influenced by MENSTRUATION. Rugh (J. T.), Penn. M. J. (Harrisburg), 1921, **25**, 261-264.

Three interesting cases are recorded in which the bone and joint symptoms were considerably aggravated during each menstrual period. In one patient with a tubercular hip, the sinus resulting from aspiration of tuberculous pus which had been closed for 2 months, burst open during a menstrual period and discharged blood for several days; this stopped with cessation of the menstrual flow. In another patient operation for villous arthritis of the knee happened to be performed the day after menstruation ceased, and a peculiar brownish synovial membrane was encountered and ten ounces of blood serum escaped from the joint—vicarious menstruation. Schuman in discussing Rugh's paper protests against operating at the menstrual period except in emergencies.—H. L.

Mental deficiency or MONGOLISM. Ward (A. C.), Med. J. Australia (Sydney), 1921, **ii.** 326.

A case report. Patient was being treated with **thyroid.**—R. G. H.

(OVARY) The use of Bohnstedt's migraine serum in gynecology [Die Verwendbarkeit des Migräneserums (Bohnstedt) in der Gynäkologie]. Abel (G.), Deutsch. med. Wchnschr. (Berlin), 1921, **47**, 1229-1230.

There seems to be a relation between attacks of migraine in women and the ovaries. French authors have even described a

"migraine ovarienne." Bohnstedt has prepared a serum from placenta (the manner of preparation is not given). He found that an intramuscular injection of this serum diminishes the activity of the ovaries and has a good influence on migraine. Abel reports good results with the use of this serum in three women. It is said to give good results also in men. (There is not a trace of real pharmacological or chemical study in the whole article. The manner of preparation of the serum is not given. The article has a decidedly commercial aspect.)—J. K.

The nerves in the human OVARY with particular reference to their termination (Uber die Nerven, insbesondere deren Endigungen, in menschlichen Eierstocke.) Akagi (Y.), Frankfurter Ztschr. f. Path. (Weisb.), 1921, **26**, 165-187.

The literature dealing with anatomical studies of nerve distribution to the ovaries is summarized as follows: They enter at the hilus with the blood vessels; there are ganglion cells in the hilus and also in the substance of the ovary; most of the ovarian nerves are vasomotor; the Graafian follicles are supplied with nerves but whether they enter the membrane granulosa is doubtful; nerve endings are numerous in corpora lutea and also in the interstitial cells. In these studies the silver impregnation methods of Ramon y Cajal and Bielschowsky were used. The ovaries of 11 human cases ranging from infancy to middle life and including cases with true and false corpora lutea were studied. It is concluded that the muscle fibers, the vessels, capillaries and especially the stroma cells are supplied with nerves. The interstitial or stroma cells are particularly rich in nerve endings. Nerve endings were found particularly abundant in the hyperplastic theca interna of atresic follicles and also in the theca interna of ordinary follicles. The terminal nerve fibres may appear as points or as bulbs—the former being more frequent. Contrary to other observers very few nerve endings were found in the superficial layer of the true and never in the false corpus luteum.—D. M.

A new proof of the internal secretion of the OVARY (Ein neuer Beweis für die innere Sekretion des Ovariums). Asher, Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1480.

Hyperglycemia caused by administration of diuretin disappears after removal of the ovaries. Parabiosis with a normal female restores the diuretin-hyperglycemia. Extirpation of the testicle has no influence.—J. K.

(OVARY) Experimental studies following oöphorectomy. Bailey (H. C.), Am. J. Obst. & Gyn. (St. Louis), 1921, **2**, 77-83.

A review of the literature. The principal deductions are that experimental work is inconclusive as regards the demonstration of

a direct effect of an ovarian secretion on the energy metabolism of the cell; that no ovarian change may be demonstrated following hysterectomy until after three or four months; that the menopause ensues even though the ovaries remain, if the **uterus** is entirely removed, and that symptoms are prevented by saving a portion of the uterine mucous membrane, so that **menstruation** may occur; and that transplantation of the ovary is of no value in relieving menopausal symptoms, unless the uterus, or part of it, remains.

—E. N.

OVARIAN sterilization at one exposure by the help of the x-rays (La stérilisation ovarienne en une seule séance à l'aide des rayons de Röntgen). Béclère (A.), J. de radiol. et d'electrol (Paris), 1921, **5**, 67.

This critical review of Béclère traces the development of the x-ray treatment of fibromyomata from its inception by Foveau de Courmelles in 1904 to the present methods by the late Professor Krönig, and continued by Seitz and Wintz. The chief part of the review is devoted to an examination of the efficacy and desirability of the German method, which consists in giving at one séance a dose of radiation which is calculated to the desired results. From a careful examination of the publications which have issued from the Fribourg and Erlangen clinics, Béclère finds a not unimportant difference in the dose which is administered at the two institutions, for what must be considered the same object. Krönig and Fredrich estimate what they call the "ovarialdosis" to be 20 per cent of the "erythemdosis," whereas the "Kastrationdosis" of Seitz and Wintz is 34 per cent of the same quantity. This difference may possibly be referable to an inequality of the standard employed at the two centres, namely, the erythema dose. The main questions raised by Béclère are two. First, can the changes in the ovary be brought about by a single application of x-rays with certainty? From an examination of published results he states that this cannot be done, and that it may therefore be necessary to repeat the exposure. The second question centers round the desirability of such single exposure methods. The economical advantage is, in his opinion, counterbalanced by the ill effects upon the patients which frequently supervene upon these prolonged exposures to x-rays, and which are not often met in the conversative method of spacing the irradiations over a considerable length of time. Béclère also discusses in some detail the arguments which have centered round the question as to whether the diminution in size of a fibroma is a sequel to the changes initiated in the ovary or whether it is due to a direct action of the rays upon the growth. The argument is well considered and the paper is a valuable one. It contains a useful bibliography, in which we fail to find the name of a single British author.—Med. Sci.

Action of OVARIAN products on the cutaneous reactions of tuberculin (Action de produits ovariens sur les cuti-réactions a la tuberculine). Bouveyron (A.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 836-837.

While the cutaneous reaction to tuberculin in young tubercular females is intensified during menstruation, various ovarian products such as the liquid from the follicles, concentrated glycerine extracts of **corpus luteum**, or the whole ovary, or the ovary deprived of its follicles and corpora lutea, completely suppresses, or attenuates the reaction. A congestive halo appears in about ten minutes, and lasts several hours, but disappears before the tuberculin reaction.

—T. C. B.

Nature of luteinic and interstitial cells of the OVARY (Sulla natura della cellula luteinica e della cellula interstiziale dell ovaio). Brugnatelli, Boll. d. soc. med. chir. di. Pavia, (Milano), 1919, —, —, Abst. Pathologica (Genova), 1921, **13**, 25.

The author made tissue cultures from the ovaries of rabbits. He obtained no growth with ovaries in a state of rest, and hardly any result from the ovaries at the end of pregnancy. Strikingly positive results were obtained from ovaries during the breeding period and at the beginning of pregnancy. The development proceeds rapidly until the tenth day, when degeneration begins to appear. The author states that the luteinic cell and the interstitial cell are not of epithelial origin, but connective, and both elements are of the same nature. He infers that these cells can be classified among the great category of adventitial cells. The hypothesis is strengthened by the periodical appearance of imposing masses of luteinic and interstitial cells in the ovary during the breeding period and the pregnancy. (See also Endocrin., **5**, 806.)—G. V.

(OVARY) Discontinuity in the morphological evolution of the chondriome of the egg of Sabellaria alveolata L (Discontinuité dans l'évolution morphologique du chondriome de l'oeuf de Sabellaria alveolata L). Fauré-Fremiet (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 986-989.

Histological—T. C. B.

Transplantation of OVARY. Fleischmann (K.), Wiener klin. Wchnschr., 1921, **34**, 621.

Data will be reported elsewhere.—J. K.

The OVARY after hysterectomy for fibroids (A follow-up study). Hawks (E. M.), Am. J. Obst. & Gyn. (St. Louis), 1921, **1**, 959-963.

The paper is based on a series of 84 cases in which a follow-up study was made. The onset of flushes was delayed when one ovary

was left and further delayed when both were left. The severity was diminished when one ovary was left and almost eliminated when both were left. Only one case had both pain and swelling in an ovary. In all the 65 cases in which one or both ovaries had been left, there were 12 subjects, or one in five, who had any trouble with the retained ovary. In 11 of the 12 it was temporary. The conclusion drawn is that it is better to leave healthy ovaries after hysterectomy for fibroids done before or near the time of the menopause.

—E. N.

Effect of undernourishment on mammalian OVARY and the sexual cycle. Loeb (L.), J. Am. M. Ass. (Chicago), 1921, **77**, 1646-1648.

Loeb reviews his investigations on this and related topics, some of which have been published in biological journals, not always accessible to medical readers. Complete excision of the **corpora lutea** leads to a notable acceleration of ovulation, though not of the process of follicular maturation. If the corpora lutea were burnt out instead of excised, ovulation was not accelerated, as the burning caused an injury of the remaining ovarian tissue and particularly of the follicles. Young follicles remained alive and even began to develop, but their vitality was much diminished, and they usually become atretic before reaching medium size. Such ovaries, characterized by the presence of only small and small-to-medium sized follicles, at a period of the sexual cycle at which there should have been present large ones, he designates as hypotypical ovaries. In these ovulation can not of course take place. Loeb has found that such a hypotypical condition of the ovaries may occur spontaneously in certain guinea pigs. A considerable number of experiments have shown also that unfavorable nutritional conditions, due either to outside factors or to a pathologic state within the animals, may be responsible for a similar condition of the ovaries. Experimental studies have shown that the follicles retrogress because the degeneration of isolated granulosa cells sets in at an early stage, and this degeneration is so pronounced that the loss of cells far exceeds their new formation. The underfeeding affects primarily the epithelial elements (the granulosa); to a minor degree the connective tissue is also affected. Recent studies by Walsh have shown that the ovum is responsible for the growth of the follicles and, ultimately, of the whole ovary. It is clear that a hypotypical condition of the ovaries is incompatible with ovulation and the normal course of the sexual cycle. The uterus in such cases usually is found to be thin and inactive.—E. N.

(OVARY) Further investigations on the origin of tumors in mice. VI. INTERNAL SECRETION as a factor in the origin of tumors. Loeb (L.), J. Med. Research (Boston), 1919, **40**, 477-496.

The experiments here reported were carried out upon mice in which had been previously followed the normal cancer rate and the cancer age through a number of generations, and in which the cancer rate and cancer age had been found to be approximately constant. Loeb concluded that "a hormone given off by the ovary regulates those tissue changes which lead to the development of cancer of the breast in mice." The influence is a quantitatively graded one. For, castration practiced at the age of 3 or 4 months completely or almost completely prevents the appearance of carcinoma of the breast in mice. In mice castrated at the age of 5 to 7 months, cancer appears, but "in all probability the tumor rate is lowered and furthermore the tumors appear later in life." In mice castrated above the age of 7 months, the frequency with which tumors appear is not markedly affected, but "possibly the age at which the tumors appear is somewhat higher." These observations suggest that the tissue changes which eventuate in the development of cancer, occur at a very early period in life, and that castration affects these primary tissue changes rather than the secondary transformation of these changes into fully developed carcinomatous growth. Prevention of breeding in mice lowers the tumor rate and raises the tumor age slightly, but its effect is not comparable to that of an early castration. Transplantation of the ovaries of the sisters into young castrated male mice belonging to strains with a high tumor rate did not lead to the development of tumors in the male mice. This Loeb interpreted as indicating that the transplanted ovaries did not function with the same completeness and in the same rhythm as normal ovaries in the female mice. The effect of hormones on the development of cancer is a specific one. A hormone influences the development of cancer only in those organs to which under normal conditions it has a specific relation. Three factors are active in the development of cancer: (a) heredity, (b) irritation (physical stimulation), (c) internal secretion (chemical stimulation). Wherein the heridity factor consists is not certain at present. Internal secretion seems to cause cancer only in co-operation with hereditary factors. On the other hand, hereditary factors need—at least in the case of certain cancers—the co-operation of hormones in a definite quantity, if cancer shall develop.—J. P. S.

The chemical composition of the OVARIES of fresh water gar, Lepidosteus. Nelson (E. E.) & Greene (C. W.), J. Biol. Chem. (Balt.), 1921, **49**, 47-56.

A report of the analysis of 12 samples of gar ovaries in which figures for lipoid, protein, water and extractive solids, ash, total nitrogen, amino nitrogen and creatine are given.—F. S. H.

Function of the OVARY during menstruation and in metrorrhagia (Intorno alla funzione dell' ovario nella mestruazione e nelle me-

trorraggie). Perazzi (P.), Folia gynaec. (Pavia), vol. XII, n. 1, abst., Pathologica (Genova), 1921, **13,** 25.

Previous researches proved the existence of specific ferments for determined proteins as shown by the Abderhalden reaction. Perazzi obtained a strongly positive reaction with ovary substrate and the serum of women suffering with so-called idiopathic metrorrhagia. Hence he postulates a relation between metrorrhagia and altered function of the ovary. The same phenomenon is found to a certain extent during menstruation.—G. V.

On the evolution of the adult OVARY of the rabbit (Sur l'évolution de l'ovarie adulte de la lapine). Salazar (A. L.), Compt. rend. Soc. de biol. (Paris), 1921, **85,** 783-784.

Of histological interest.—T. C. B.

A case of OVARIAN tumor in a mulatto. Stone (I. S.), Washington M. Ann., 1918, **17,** 253.

Not of endocrine interest.—E. N.

OVULATION and MENSTRUATION as post-operative considerations. Watkins (T. J.), Am. J. Obst. & Gyn. (St. Louis), 1921. **2,** 489-493.

Ovulation and menstruation as post-operative considerations are important because many of the pelvic operations affect these functions. The usual good health which obtains after the menopause demonstrates the ability of the endocrine glands to compensate for the loss of ovarian secretion. The author believes that the difference in severity between the neuroses of the natural and the artificial menopause is negligible. He advocates the conservation of the ovaries whenever possible in cases of uterine fibroids and salpingitis. Conservation of menstruation has no value aside from its relation to reproduction. The function should be abolished by excision of the body of the uterus in the course of abdominal pelvic operations when conditions obtain which make pregnancy impossible or inadvisable.—E. N.

Researches on the function of the PANCREAS (Untersuchungen über die Funktion des Pankreas). Adler (L.), Arch. f. exper. Path. u. Pharmakol. (Leipzig), 1921, **91,** 110-124.

The temperature-raising and awakening effects of **thyroid** extract upon the hibernating hedge-hog is lessened or entirely destroyed if the animal is treated with pancreas extract from another hibernating animal. A similar retarding influence is exerted upon **thymus** extract or **adrenin** by administration of pancreas extract. —W. J. A.

(PANCREAS) Un médicament usuel: l'opothérapie pancreatique. Faroy (G.), Prog. méd. (Paris), 1921, **36**, 361-362.

A review in which it is concluded that so far as internal secretion is concerned, pancreas preparations are useless except, perhaps, in certain cases of "hyperhepatic diabetes."—R. G. H.

The essential atrophy of the PANCREAS. Oertel (H.), J. Med. Research (Boston), 1919, **40**, 289-294.

Under this title Oertel describes a lesion of the pancreas in which "quantitative loss and collapse of parenchyma are the only essential elements and occur independently of either vascular or inflammatory changes or an increase in fibrous connective tissue." The writer has observed five cases. All of these patients had a severe, even acute, diabetes, ending in coma and death.—J. P. S.

Toxic necrosis and regeneration of the acinar cells of the PANCREAS. Parker (F., Jr.), J. Med. Research (Boston), 1919, **40**, 471-476.

"Toxins which cause lesions of the heart, liver, kidney and adrenal, cause similar lesions in the acinar cells of the pancreas, which have heretofore been overlooked. The acinar cells of the pancreas have great powers of regeneration." Arsenic was found to cause necrosis of the pancreas as well as of the liver, kidney and adrenal.—J. P. S.

Action of PANCREATIC extract injected into the blood of a diabetic animal (Action de l'extrait pancréatique injecté dans le sang, chez un animal diabétique). Paulesco, Compt. rend. Soc. de biol. (Paris), 1921, **85**, 555-557.

The chief symptoms of total extirpation of the pancreas are an augmentation of the proportion of sugar in the blood and urine; an augmentation of the proportion of urea in the blood and urine; an augumentation of the acetone bodies in the blood and urine. The intravenous injection of pancreatic extract causes a diminution or even a transient suppression of the hyperglycemia and glycosuria; a diminution or transient suppression of the urea in the blood and in the urine; a notable diminution in the acetonemia and acetonuria. Tables of experimental results are given.—T. C. B.

Influence of lapse of time after the intravenous injection of PANCREATIC extract in a diabetic animal (Influence du laps de temps écoulé depuis l'injection intraveineuse de l'extrait pancréatique chez un animal diabétique). Paulesco, Compt. rend. Soc. de biol. (Paris), 1921, **85**, 558.

The effect of pancreatic extract on the glycemia and glycosuria commences immediately after the injection, attains a maximum in about 2 hours, and lasts about 12 hours.—T. C. B.

Influence of the quantity of PANCREAS employed in preparing the extract for injection into the blood of a diabetic animal (Influence de la quantité de pancréas employée pour préparer l'extrait injecté dans le sang chez un animal diabétique). Paulesco, Compt. rend. Soc. de biol. (Paris), 1921, **85**, 558-559.

The effect of the extract varies with the quantity of gland employed.—T. C. B.

Action of PANCREATIC extract injected into the blood of a normal animal (Action de l'extrait pancréatique dans le sang chez un animal normal). Paulesco, Compt. rend. Soc. de biol. (Paris), 1921, **85**, 559.

Pancreatic extract injected into the jugular of a normal dog, caused a diminution in the blood sugar, as well as in the urea of the blood and urine.—T. C. B.

Xanthomatosis in a case of recurrent PANCREATITIS (Ueber Xanthomatose in einem Fälle rezidivieren der Pankreatitis). Wynhausen (O. J.), Berl. klin. Wchnschr., 1921, **58**, 1268-1270.

An interesting case. A very fat man, who was intemperate in eating and drinking and who had cases of diabetes in his family twice received a severe trauma on the abdomen. First he developed a general xanthomatosis, this receded and recurred from time to time. During such an attack the cholesterol content of the serum was enormously increased. The xanthomata disappeared when the patient took only a little fat and reappeared when he took much fat. At the same time he had attacks of glucosuria and of a disturbed external function of the pancreas (undigested muscle fibres but no fat in the stools). It is probable that the pancreas has a certain relation to the cholesterol metabolism.—J. K.

The comparative effects of PARATHYROID and THYROID feeding on growth and organ hypertrophy in the white rat. Cameron, (A. T.) & Carmichael (J.), Am. J. Physiol. (Balt.), 1921, **58**, 1-6.

At the present time there is a tendency to consider the actions of thyroid and parathyroid as opposite in nature. Thyroid feeding inhibits growth in young white rats, and causes hypertrophy of various organs. The present study has to do with the effect of parathyroid feeding on growth and hypertrophy of the organs. The experiments were carried on with the usual technique. Six rats developed tetany. The results show that even very heavy doses of parathyroid produce no definite effect on growth, and no organ-hypertrophy.—T. C. B.

A discussion of the PARATHYROID question with particular emphasis on the acidophilic cell (Beitrag zur Epithelkörperchenfrage, unter besonderer Berücksichtigung der Acidophile der Zelle). Koopman (H.), Frankfurter Ztschr. f. Path. (Weisb.), 1921, **25**, 342-372.

The author has studied the morphological appearance of the parathyroids in 261 cases, including six cases of paralysis agitans. He confirms work of the most recent observers that there are no characteristic pathological changes in the parathyroids of paralysis agitans. He reviews briefly the commoner alterations found in the parathyroid as hemorrhage in infancy, hypertrophy and hyperplasia in rickets and osteomalacia, adenoma, and then goes into a discussion of the occurrence of the acidophilic cells of the gland. As is well known, these acidophilic cells may occur singly and in groups scattered irregularly through the gland. In the 255 cases grouped according to age, he found the frequency of acidophilic tissue to increase with age. Thus, of 36 cases in the first decade of life, none showed acidophilic cells; of 12 cases in the second decade there were 2; of 30 cases in the third decade there were 12; of 41 cases in the fourth decade there were 16; of 34 cases in the fifth there were 18; of 23 cases in the sixth, 16; of 40 cases in the seventh, 23; of 27 cases in the eighth, 23, and of 12 cases in the ninth decade of life there were 9 cases with acidophilic cells. He thus confirms the generally accepted opinion that the acidophilic cells in the human parathyroid are rarely seen before puberty, then the frequency progressively increases with each decade. He points out that Erdheim, using morphologic methods, had found these acidophilic cells poorer in lipoids than the basophilic types and his observations bear this out. He thinks the acidophilic cells may be considered the morphologic expression of the internal secretory activity of the gland.—D. M.

The treatment of tetania PARATHYREOPRIVA (Über die Behandlung der Tetania parathyreopriva). Eiselsberg (A.), Wiener klin. Wchnschr., 1922, **35**, 1-2; München. med. Wchnschr., 1921, **68**, 1540.

In 20 years the author carried out 2588 strumectomies with 6 fatal cases of tetany. The treatment of this form of tetany consists in administration of parathyroid tablets (3-4 daily), calcium lactate up to 30 grams daily, afenil intravenous during the attacks, clysters with chloral and a diet without flour. Only in cases in which this treatment proves unavailing should grafting be tried.—J. K.

(PARATHYROID) Muscle tonus. II. The point of attack of guanidine and methylguanidine in the production of motor irritability. Guanidine-cocaine antagonism. Frank (E.) & Stern (R.), Arch. f. exper. Path. u. Pharm. (Leipzig), 1921, **90**, 168-179.

An antagonism between guanidine and cocaine (or novocaine) was demonstrated in the frog. Experiments on the response to electrical stimuli after guanidine intoxication indicate that guanidine acts upon the "receptive substance" of the sarcoplasm and not upon the muscle substance in general. Synthetically prepared methylguanidine acts qualitatively exactly as guanidine.

—Chem. Abst.

(PARATHYROID) Paralysis agitans. Jakob, Berl. klin. Wchnschr., 1921, **58**, 1393-1394.

Demonstration of a patient with Parkinson's disease, markedly improved by suggestion. This is cited as disproving the significance of the case of endocrine "cure" of Parkinson's disease reported by Kühl. (See abstract in this issue.)—J. K.

(PARATHYROIDS) Paralysis agitans. Kühl, Berl. klin. Wchnschr., 1921, **58**, 1393.

Demonstration of a patient with Parkinson's disease, markedly improved after implantation of a parathyroid.—J. K.

Hyperplasia of the PARATHYROIDS in human rickets. Pappenheimer (A. M.) & Minor (J.), J. Med. Research (Boston), 1921, **42**, 391-403.

A careful histologic study was made upon parathyroid glands from 14 children with rickets and 18 non-rachitic children. Glands of children of corresponding ages were compared. There was found a very definite increase in the size of these glands in children with rickets. This increase in size was due to actual multiplication of the cells and not to an increase in size of the individual cells. The parathyroids of children within the first 18 months of life consist almost entirely of "plant-like cells with very clear unstained cytoplasm, round large nuclei, and clear cell outlines." In rickets there was no constant nor characteristic change in the cell type, and the clear cell remained markedly predominant. In this series of cases there was no increase in the supporting tissue of the parathyroids in rickets, and no increase in the vascular supply or congestion of the blood vessels not found equally in non-rachitic patients. The state of nutrition of the child had no bearing on the size either of the gland as a whole or of its individual elements.—J. P. S.

PARATHYROID gland changes in rickets and other diseases of bone (Uber Epithelkörperchenbefunde bei Rachitis und anderen Knochenerkrankungen). Ritter (C.), Frankfurter Ztschr. f. Path. (Weisb.), 1920, **24**, 137-176.

This paper reviews the morphologic changes found in the parathyroids in cases of rickets, osteogenesis imperfecta, osteomalacia,

and Moeller-Barlow's disease, coming to post-mortem examination in the Pathologic Institute at Freiburg. In rickets the parathyroids are often slightly enlarged, hyperemic, edematous and occasionally showing increase in the stroma. The enlargement is less common in early cases than in long standing severe rickets. In Moeller-Barlow's disease (one case) the parathyroids were normal. In osteomalacia and osteoporosis, the parathyroids were never found atrophic but often enlarged. In one case of osteomalacia the clear vegetable-like cells predominated, but in all the others the darker, more basophilic type predominated, just as in the cases of long standing and severe rickets. In general his observations confirm those of Erdheim.

—D. M.

(PARATHYROID) Experiment in new method of therapy of paralysis agitans. Weinberg (M. H.) & Schubb (T.), Soc. Exper. Biol & Med. (N. Y.), 1921, **19**, 21.

Starting out from the premises that paralysis agitans is due to hyperparathyroidemia, as advocated by several observers, we proceeded to prepare a parathyroidectin substance for the treatment of this condition. Experiments were conducted on rabbits and on goats. The two external parathyroid glands of the goat were removed, and after forty days the blood of the goat was withdrawn and glycerinized. The administration of this blood to Parkinsonian patients seems to show promising results. Further study of this method of therapy is now under way.—Quoted.

PERSPIRATION in man (Beobachtungen über die Schweiszsekretion beim Menschen). Peller (S.) & Strisower (R), Wiener Arch. f. inn. Med., 1922, **3**, 297-308.

Many patients with **diabetes** perspire very little or not at all. Aspirin or pilocarpin do not cause perspiring. When **adrenalin** or **thyroidin** are given with aspirin or pilocarpin in diabetes perspiring occurs. This is not due to suggestion, as the combination of aspirin or pilocarpin with a solution of NaCl is inactive. Perspiring is independent of the amount of water in the body. Patients with hypothyroidism also show a raised perspiration after the administration of thyroidine. It is highly probable that the perspiring is regulated by endocrine processes via the autonomic nervous system.

—J. K.

The functional effects of the PINEAL gland and its tumors (Die Zirbel und ihre Tumoren in ihrem funktionellen Einfluss). Askanazy (M.), Frankfurter Ztschr. f. Path. (Wiesb.), 1920, **24**, 58-77.

This paper discusses the morphology of pineal gland tumors, the function of the pineal gland and points out the possible cor-

relations of the pineal gland particularly with the sex glands. Teratomas and cysts are the most common forms of "tumors." The literature reports show that many of these cases have shown precocious sexual development and in support of this clinical observation some of the experimental work is reviewed, especially that with fowls in which removal of the pineal gland resulted in enlarged sex glands.—D. M.

Primary tumors of the PINEAL gland (Uber primäre Tumoren der Zirbeldrüse). Giebel (W.), Frankfurter Ztschr. f. Path. (Weisb.), 1921, **25**, 176-190.

Reports the clinical and autopsy findings of two patients with tumors of the pineal gland. In one of these was a sarcoma in a male, aged 25 years. This tumor was of indefinite morphology and on account of the lymphocytic and eosinophilic infiltration and polymorphic type of the tumor cell a more specific classification could not be suggested. In fact, it was due to its staining characteristics with Van Giesen's and Mallory's connective tissue stains that it was grouped as a sarcoma. The second was a walnut-sized dermoid cyst in a boy aged 15 years. This patient clinically had vague symptoms of brain tumor, unlocalizable. The literature is reviewed and, including the above two cases, there are reported 53 primary tumors grouped as follows: Sarcomas, 13; teratomas, 10; cysts, 7; hyperplasias, 7; gliomas, 5; psammomas, 3; carcinomas, 3; angiomas, 1; undetermined nature, 4.—D. M.

The action of PLACENTAL and TESTICULAR lipoids on the male and female sex-organs (Ueber die Wirkung des Placentär—und Hodenlipoids auf die männlichen und weiblichen Sexualorgane). Fellner (Otfried O.), Arch. f. d. ges. Physiol. (Berlin), 1921, **189**, 199-214.

Injection of placental and ovarian lipoids produces a diminution of testes, especially shrinking of canals. In ripe rabbit testes spermatogenesis ceases, and the sperm cells degenerate. Detritus-type masses form in the lumina. Degeneration also takes place in unripe cells. Interstitial tissue increases. Signs of epithelial degeneration are seen in the epididymus. Testicular lipoids produce similar effects. The action is not specific since other lipoids produce it. Testes of new-born children show similar appearances, similarly to be referred to placental lipoids of the mother. Seminal vesicles and prostate do not appear to be affected macroscopically. Testicular lipoids show the same physiological properties when injected into females as do ovarian and placental lipoids; enlarged uterus with numerous deep glands, and enlarged mammae. This growth-producing action is specific. It is considered probable that the active chemical substance in these lipoids is identical. The

author reviews the evidence in an endeavor to ascertain which cells produce these lipoids.—A. T. C.

Internal secretion of PLACENTA (Ueber die innere Sekretion der Plazenta). Puppel (E.), Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1294-1295.

The author prepared what he called a placenta-opton, made by allowing the placenta to undergo sterile autolysis. The preparation appears to be of value in obstetrics because of its effect in stimulating uterine contraction. It has no galactogogue effect. In one case of sterility it was injected, with successful results; in a second, it failed. Good results were obtained in two cases of dysmenorrhea.
—J. K.

(PLACENTA) Experiments on animals with placenta-opton (Tierversuche mit Plazenta-Opton). Kratzeisen, Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1260.

Five c.c. of 5% solution of placenta-opton was injected subcutaneously every two days into young guinea pigs and albino rats. When 30 cc. had been given the animals were killed. The mammae were found to be larger than in the controls and the uterus and vagina were nearly always double the normal size. The wall of the uterus showed hypertrophy of the muscle fibers; the epithelium also was thicker and the number of glands increased. Similar experiments reported by other authors have generally been accompanied by a hemorrhagic nephritis. This Kratzeisen could not confirm. It must be borne in mind that other experimenters have employed ether and alcohol extracts.—J. K.

Experimental studies on the toxicity of PLACENTAL lipoids in their relation to the etiology of puerperal eclampsia (Experimentelle Untersuchungen über die Toxizität von Placentalipoiden, mit Bezug auf die Aetiogenese de Puerperal-eklampsie). Schönfeld (H. E. H.), Arch. f. Gynäk. (Berlin), 1921, **115**, 80-125.

A characteristic review of the literature. Personal experiments of S. yield the conclusions that the alcohol, acetone and glycerin extracts of the placenta contain constrictor toxins which are thermolable and insoluble in ether. They act electively on liver cells, but are also toxic for kidney cells, and vascular endothelium. The nucleus is primarily affected. There was observed a constrictor, a thrombosis producing, a partuition facilitating and a liver, kidney and endothelial poison in the extracts. The relation between these toxins and eclampsia is stressed.—F. S. H.

Retarded RICKETS and starvation osteopathy (Spätrachitis und Hungerosteopathie). Simon (W. V.), Veröffentlichungen aus dem Gebiete der Medizinalverwaltung (Berlin), 1921, **14**, 351-443.

The osteopathy seen during and after the war is not a new disease, but belongs in the group of rickets and osteomalacia. This form of "Kriegs-osteopathie" is due to a **pluriglandular** insufficiency. The author considers the **skin** as an endocrine structure and especially as a **chromaffin organ.** Thus perhaps may be explained the fact that these diseases are seen especially in places and houses where there is not enough light. This explains also perhaps the splendid effect of the treatment of rickets with artificial sunlight. The causes of the "Hungerosteopathies" are (1) Defective feeding; (2) Intoxication; (3) Influences on the skin (want of light, dirt, etc.). The best treatment is: phosphorus-cod liver oil, calcium, **adrenalin,** strontium lactate, fresh air, light and massage.—J. K.

Treatment of SCLERODERMIA with x-rays (Zur Röntgenbehandung der Sklerodermie). Donath (J.), München. med. Wchnschr., 1921, **68,** 1326-1327.

The author believes that the **thyroid** plays an important part in this disease. It is specially a hypofunction of this gland. In two cases he observed improvement by giving thyroid. X-rays when they have a good effect must stimulate the thyroid and not as Hammer in a previous paper stated decrease its function.—J. K.

SECRETIN. V. Its effect in anemia, with a note on the supposed similarity between secretin and vitamin B. Downs (A. W.) & Eddy (N. B.), Am. J. Physiol. (Balt.), 1921, **58,** 296-300.

Fully grown rabbits were fed on a diet consisting exclusively of polished rice until the blood count fell to four million. They were then put on a full diet of oats, turnips, carrots and cabbage. One group of six rabbits received in addition a subcutaneous injection of 20 mgm. per kilo body weight of dried secretin in saline solution. A second group of four controls received like injections of saline solution only. All the animals improved in weight and blood count, but the secretin animals showed an increase of 27.3 per cent over the normal blood count at the end of the eighth week, while the controls had barely reached the normal. The secretin group showed an average increase of 145 gms. above the original weight, while the controls were 108 gms. below the original. Could this marked improvement be brought about by an equivalent excess of water soluble vitamin? Five rabbits were injected with secretin. Within an hour the blood count had increased 17.55 per cent, and the second count was still higher. Five other rabbits were injected with equivalent amounts of vitamin from brewer's yeast. The blood count remained about the same as before injection. The number of red cells in circulation was not increased.—T. C. B.

Anatomical modification of the SPLEEN following THYROIDECTOMY (Le modificazioni anatomiche della milza consecutive a

tiroidectomia). Baggio (Gino), Arch. di Fisiol. (Florence), 1921, **19,** 89-100.

Rabbit spleens show a considerable reduction of weight (absolute and relative) following thyroidectomy. The atrophy of the organ is not accompanied by any particular alteration of structure. It is directly related to the course and origin of the general cachexia or the organism, and its extent is parallel to the former.—A. T. C.

Anatomical modifications of the SPLEEN following stimulation (Le modificazioni anatomiche della milza consecutive a stimolazione). Baggio (G.), Arch. di Fisiol. (Florence), 1921, **19,** 299-315.

Spleens of rabbits stimulated daily for periods varying from 20 to 80 days showed in 78 per cent of the cases a diminution of weight averaging 0.182 gm., usually accompanied by a diminution of body weight. Thyroidectomy produces similar results (Baggio, Arch. di Fisiol., **19,** 89). No definite histological changes were detected. The number of lymphocytes was diminished.—A. T. C.

SPLENIC syndromes. Mayo (W. J.), Surg. Clin. N. Am. (Phila.), 1921, **1,** 1307-1325.

A survey of five syndromes illustrating the fact that pathologic conditions found in the **spleen** are obviously closely related to the pathology of the blood. Reports of cases of splenic anemia, hemolytic **icterus,** pernicious anemia, polycythemia, and splenomyelogenous leukemia, in all of which splenectomy was performed are detailed. The author reminds us that the spleen, while concerned with the purification of the blood, with the filtration from the blood of worn-out red blood cells and infectious and toxic material, and their direction to the liver, is not the principal but rather an agent. Twelve out of 270 splenectomized patients could be put into no known classification. The author concludes that it is best at this time to regard the spleen as little known territory, through which a few trails have been blazed.—C. R.

The correction of STERILITY. Maier (F. H.), The Penn. M. J. (Harrisburg), 1921, **25,** 78-82.

After discussing the several anatomic abnormalities, infectious and other pathological causes of sterility, mention is made of the endocrinopathic origin. The latter may be of ovarian nature, or due to pre- or post-adolescent **thyroid** or **pituitary** insufficiency. Usually obesity and amenorrhoea accompany the sterility in females. When the correct origin is determined the appropriate gland extract, thyroid, pituitary or **corpus luteum** may occasionally cure the sterility. The outlook is better if one can recognize the mild forms of endocrine deficiency when organotherapy is more promising. In discuss-

ing the above paper, Jump and Anspach agree in the main with the author's remarks, but sound a note of caution in expecting too much from ductless gland extracts at the present time.—H. L.

Certain dietary factors in the causation of STERILITY in rats. Reynolds (E.) & Macomber (D.), Am. J. Obst. & Gyn. (St. Louis), 1921, **2**, 379-394.

Careful studies by means of deficiency diets of one type or another led the authors to the following conclusions: A moderate decrease in the percentage of the fat soluble vitamine, of the protein, or of the calcium contained in an otherwise excellent diet produces a definite decrease in the fertility of individual rats. A slight decrease in the fertility of both partners will produce a sterile mating. The fertility of the mating may be stated as the product of the fertility of the individuals concerned. If the index so obtained falls below a given point the mating will be sterile, and this result holds true whether the partners are of equal or of widely different fertility. These principles explain the fact that two individuals which are sterile when mated together may nevertheless reproduce freely if mated to new partners (of higher fertility). Dietary deficiencies produce a lowered fertility which varies in degree with different individuals, though of the same parentage and in the same cage. Diminished fertility sometimes results in the appearance of abortion. More percentage deficiency in both proteins and calcium produces visible ill health and great infertility.—E. N.

(TESTES) Conditions determining the secondary SEX characters in the Urodela (Sur le conditionnement des caratères sexuels secondaires chez les Batraciens Urodéles). Aron (M.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 482-484.

Histological discussion of the paratesticular tissue as the homologue of the interstitial tissue in mammals.—T. C. B.

(TESTES) On the structure of the wall of the seminiferous tubules (Sur la structure de la paroi propre des canalicules séminipares). Bologa (V.) & Goldner (J.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 586-588.

Histological.—T. C. B.

Presence of TESTIS and uterus in the hernial sac of a man (Presenza di utero e testicolo nel sacco erniarion di un uomo). Bolognesi (G.), Arch. f. klin. Chir. (Berlin), May, 1921; Abst., Pathologica (Genova), **13**, 549.

In the hernial sac of a left inguinal hernia of a male otherwise offering a normal development of all the other external sexual characteristics, an undescended testis has been found and an infantile uterus with tube. The testis offered the characteristics of

cryptorchidism. The uterus and tube were rather developed. The author points to the noteworthy persistence of embryonal duplicity. Only one sexual gland had been found, but the local operation does not exclude the presence of ovary in the patient. The most interesting feature of the case is the relatively good development of uterus and tube.—G. V.

(TESTES, PROSTATE) Is rejuvenation after prostatectomy a Steinach effect (Ist die Verjüngung nach der Prostatektomie als Steinacheffekt aufzufassen)? Blum (V.), Wiener klin. Wchnschr., 1922, **35**, 2-4.

It is often observed that after prostatectomy the patient appears younger. Is this caused in the same way as Steinach's rejuvenation? Steinach and his pupils state that prostatectomy is followed by an obliteration of the ducti ejaculatorii. This, however, is not only not true, but when after a prostatectomy the ducti ejaculatorii are obliterated this must be considered as due to a serious breach of technic by the surgeon. If Steinach were right the hypertrophy of the prostate, which compresses the ducti ejaculatorii, ought to give rejuvenation. The term "hypertrophy" of the prostate as generally used is incorrect. It is much better to call it an adenoma of the prostate. It is remarkable that this adenoma contains a substance, which, when injected into dogs, causes intoxication and death. In normal prostates this substance is not found. In the same way in the blood of patients with prostatic hypertrophy eosinophilia is found. This disappears after the operation. It is, therefore, much more probable that the rejuvenation after removal of the adenoma is due, not to an obliteration of the ducti ejaculatorii, but to the removal of a tumor having a toxic influence on the organism.—J. K.

(TESTES) On the conditions determining the secondary SEX characters in fishes (Sur le conditionnement de caractéres sexuels secondaires chez les Poissons). Courrier (R.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 486-488.

Is there in the fishes an interstitial gland as in mammals, and if so does it influence the secondary sex characters? The stickleback was chosen for a solution of this question because it has at the time of reproduction well marked secondary characters. Its ventral surface becomes a scarlet red, and the kidneys are transformed; the nephrocytes are charged with large secretory granulations which furnish an abundance of mucus. An histological study of the testicle before and during reproduction shows a testicular interstitial gland, but it differs from mammals in being limited to a certain period of the year.—T. C. B.

On the existence of an interstitial gland in the TESTICLE of fishes (Sur l'existence d'une glande interstitielle dans le testicule des

poissons). Courrier (R.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 939-941.

Chiefly histological, showing the existence of interstitial glands in the testicles of a number of species of fish.—T. C. B.

Vitamine studies. VII. The influence of fresh alfalfa upon the weight of TESTES in single-comb white leghorn cockerels. Dutcher (R. A.) & Wilkins (D. D.), Am. J. Physiol. (Balt.), 1921, **57**, 437-443.

Not of endocrine interest.—T. C. B.

Sarcomatous abdominal TESTICLE in a hermaphrodite. Halpenny (J.) & Kinneard (G.), Canad. M. Ass. J. (Montreal), 1921, **11**, 632.

The writers cite Swale Vincent and Bouin and Ancel to prove that the essential for a hermaphrodite is not spermatozoa and ova, but the presence of the internal secretion of both testicle and ovary. The article reports a case clinically described as a hermaphrodite. The diagnosis of a large abdominal tumor lay between a fibroid uterus and a sarcomatous testicle. At operation it was proven to be the latter, by a specimen removed for section. No ovary was found. It is suggested that an abdominal testis is more liable to malignancy than is the scrotal organ. Therefore, if it cannot be placed in the scrotum by operation, its ablation is indicated. It is doubted if any surgical transplantation of testis or ovary can be so successfully carried out that a hermaphrodite can be converted into a creature having distinctive sex characteristics.

—Author's Abst. (J. H.)

(TESTES) Criticism of rejuvenescence according to Steinach (Critique du rajeunissement selon Steinach). Hanak (A.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 698-699.

If the development of the attributes of virility, and the sexual character in the male is regulated by the testicles, we must ask if it is possible to restore these attributes and the sexual instinct in an individual with senile atrophy of the testicles. If the testes produce an excitant for the anaplastic phase of development, whence comes the excitant for the cataplastic phase? The problem of rejuvenescence is strictly linked to that of senescence.—T. C. B.

Changes in transplanted TESTES (Ueber das Schicksal frei transplantierten Hoden). Kleeberg, München. med. Wchnschr., 1921, **68**, 1133.

The experiments were made in guinea pigs. The cells of the seminal epithelium become necrotic. Twenty days after transplantation the whole organ is generally necrotic and granulation

tissue has begun to grow from the periphery to the center. The invading cells look like macrophages and contain much fat. Cholesterol is not present. The interstitial cells do not increase in number or volume, but become necrotic like the seminal cells. The author does not believe that the transplanted glands assume any special endocrine function.—J. K.

(TESTES) On the retardation of masculinisation after partial castration (Sur le relentissement de la masculinisation dans la castration partielle). Lipschütz (A.), Ottow (B.) & Wagner (Ch.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 630-632.

After partial castration, a retardation of development of the sex characters has been occasionally observed. One could think of this as due to a diminished internal secretion, but such a theory is not in accordance with observed fact. Guinea pigs also show this, but examination proves that the remaining fragment of testicle has degenerated, cicatrized or even disappeared. This was not the case in the rabbits. The remaining fragment was in a state of development corresponding to the age of the animal at the time of operation. As the mass of testicle left in situ (one-quarter to one-half of one testicle, the other being entirely removed) was sufficient for normal masculinisation, we must explain the sexual infantilism as due to the **infantilism** of the remaining testicular fragment. **Eunuchoidism** is caused either by infantilism or retrograde development or complete destruction of the respective tissues of the testicle.

—T. C. B.

The prostate and roentgen exposure of the TESTICLES. Neménow (M.), Ztschr. f. Urol. (Berlin & Leipzig), 1921, **15**, 45-49.

Neménow experimented on dogs and found that the prostate became enlarged after exposure of the testicles to the roentgen rays. The seminiferous cells in the testicle atrophied while the Leydig cells proliferated, and he theorizes that the latter—as the producers of the internal secretion of the testicle—secrete more profusely as they proliferate and this excessive secretion entails the hypertrophy of the prostate. This is analogous to clinical experience: As spermatogenesis dies out in elderly men, the Leydig cells proliferate and the prostate hypertrophies secondarily, as in the experiments on dogs, the microscopic changes in the testicles being identical. He is now making microscopic examination of the testicles and prostate in elderly cadavers to see whether they sustain his view. It warns, he adds, of the need of caution in accepting Steinach's operation which, unfortunately, he continues, was published too early.

—J. Am. M. Ass., **78**, 157.

Spontaneous disappearance of certain secondary SEX characters in a cock. Histological study of the TESTICLE (Disparition spon-

tanée de certains caractères sexuels secondaires chez un coq. Étude histologique du testicule). Portier (P.) & de Rorthays (Mlle. R.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 444-446.

A cock hatched in June, 1919, developed normally as regards sexual instinct and secondary sex characters. One year later, in June, 1920, there began a rapid modification: he became "triste," ceased to crow, isolated himself in one corner of the barnyard, and was indifferent to the presence of the female. He died in August, and the testes were found to measure only 12 mm., the size of the normal at two months. Their weight was 0.6 gm., where the normal varies between 14 and 40 gms. The histology of the testicles is given, showing a return to the embryonic condition. These facts confirm those obtained experimentally by ablation of the testicles. Attention is called to the fact that the total weight of the tesicles is near the inferior limit which Pezard estimated to be essential for development of the secondary sex characters.—T. C. B.

Senile changes of the TESTIS and prostate in dogs. Smith (L. W.), J. Med. Research (Boston), 1919, **40**, 31-50.

Simple senile atrophy of the testicle from vascular sclerosis is entirely lacking as a pathological entity. Testicular atrophy is accompanied by epithelial, mesothelial and endothelial changes. These may be degenerative or proliferative. The epithelial changes, when degenerative, begin centrally in the tubules; when proliferative they begin usually with the basal cell layer of spermatogones. The mesothelial changes are usually proliferative and show an increase of either the interstitial cells or the connective tissue stroma or both. The endothelial changes, when degenerative, are sclerotic and are indicative of atrophy; when proliferative they are usually an accompaniment of tumor formation. Senile testicular tumors are apparently of two general types: those derived from the epithelium of the tubules, and those derived from the interstitial cells. The cells of these tumors all show a tendency toward the undifferentiated prepubertal type of cell development, with the power of mitosis in growth, but not in differentiation and specialization. Epithelial changes are localized primarily in single tubules. Several adjoining tubules may become involved by extension or fusion with a resultant single tumor nodule or with an apparently focal area of atrophy. The usual epithelial atrophy is a mucoid degeneration of the cytoplasmic elements, beginning centrally in the tubules. The interstitial cell in senility undergoes a characteristic diminution in size with an accumulation of large brownish pigment granules and the gradual obliteration of its lipoid content.—J. P. S.

Modern views on the transplantation of TESTICLES (Der gegenwärtige Stand der Hodenüberpflanzung). Stabel, Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1248.

In six cases of homosexuality the author has transplanted a testicle, but has never seen any good result from it.—J. K.

(TESTES) The experiments of Regnier de Graaf and the functions of the seminal vesicles (L'experience de Régnier de Graaf et les fonctions des vésicules séminales). Wertheimer (E.), & DeBois (Ch.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 504-505.

Not of endocrine interest.—T. C. B.

Clinical and pathological aspects of TETANY (Beiträge zur Klinik und Pathologie der Tetanie). Elias (H.) & Spiegel (E. A.), Wiener Arch. f. inn. Med., 1921, **2**, 447-460.

In human tetany the inorganic phosphorus content of the serum is increased. The phosphorus of the lipoids does not change. In serious cases the inorganic phosphorus content is often higher than in slight cases. There are, however, exceptions. The increased amount of phosphorus is certainly not due to the contractions or spasms of the muscles. The hyperphosphoremia seems to be an important symptom of tetany.—J. K.

A case of spindle cell sarcoma of the THYMUS with discussion of the occurrence and importance of glandular elements in the thymus (Ein Fall von Spindelzellensarkom der Thymus, zugleich ein Beitrag zur Frage und Bedeutung des Vorkommens drüsiger Elements in der Thymus). Brand (O.), Frankfurter Ztschr. f. Path. (Weisb.), 1920, **24**, 445-465.

This paper reports the case of a male, aged 28, dead of cerebro spinal syphilis in which a mediastinal mass had been recognized during life and a clinical diagnosis of gumma of the pericardium made. The post-mortem examination showed an encapsulated tumor mass 9x7x3 cm. in the lower pole of the thymus area. Microscopic examination showed it to be a spindle cell sarcoma rich in blood vessels—a kind of angiosarcoma. There were numerous elongated branching glandular spaces lined with cuboidal and columnar epithelium. Outside the tumor mass definite thymic tissue with formed Hassall's corpuscles were present. These glandular spaces are probably the remnants of the embryological ducts of Remak from whose involution many believe the Hassall's corpuscles are formed. It is suggested that the tumor arose from a portion of the fetal thymus which during development failed to differentiate into normal thymic tissue.—D. M.

Various appearances of the hepatic cell in the tadpoles of Rana temporaria fed with THYROID (Divers aspects de la cellule hépatique chez les têtards de Rana temporaria nourris avec de

la thyroïdes). Dragoiu (J.) & Fauré-Fremiet, Compt. rend. Soc. de biol. (Paris), 1921, **85**, 434-436.

Histological.—T. C. B.

The phenomena of caryorrhexis in the human THYMUS (Les phénomènes de caryorhexis dans le thymus humain). Dustin (A. P.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 1103-1105.

Histological.—T. C. B.

(THYMUS, THYROID) Modification of germplasm by hormones (Versuche über Keimesänderung durch Inkreteinflusz). Grote (L. R.), Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1461-1462.

The author gave to male and female mice **thymus** opton or **iodothyrin.** He observed that the offspring of father, mother or both that had been treated with thymus opton showed a retarded growth, though they were born with a normal weight. The young of animals to which iodothyrin was given grew in some cases more rapidly than the control animals; in another case the growth was normal.—J. K.

The question of the small THYMUS cortex cell (Zur Frage der kleinen Thymusrindenzellen). Pinner (M.), Frankfurt. Ztschr. f. Path. (Weisb.), 1920, **23**, 479-498.

Discusses the old question of the origin and nature of the small lymphocytic cell of the thymus. Are they of endodermal or of mesoblastic origin? Concludes with the majority of recent authors that these cells may be identified with true blood lymphocytes.

—D. M.

On the THYMUS (Over de thymusklier). Lebeer (J.), Vlaamsche geneesk. Tijdschr. (Gent), 1921, **2**, 400-410.

An excellent review. The author points out that it has never been proved that the thymus is an endocrine organ. He considers it probable that it has something to do with the regulation of nuclein metabolism.—J. K.

Gland physiology. XLVII. The relation between THYMUS, spleen and bone-marrow (Beiträge zur Physiologie der Drüsen. XLVII. Mitt. Leon Asher. Die Beziehung zwischen Thymus, Milz und Knochenmark). Matsuno (G.), Biochem. Ztschr. (Berlin), 1921, **123**, 27-50.

Rabbits of nearly the same age and size were used in these experiments. No particular diet was fed. The animals were bled, splenectomized or thymectomized, or combinations of the operations were done and the effect of these procedures on the bone-marrow studied by hemoglobin, erythrocyte and leucocyte counts on the

blood. The effect of the administration of HCN on control and test animals was also determined. Extensive protocols and charts are given. The conclusion is made that the thymus exerts a stimulating influence on bone-marrow. The removal of the spleen does not alter the picture produced by thymectomy.—F. S. H.

(THYMUS) Concerning status thymo-lymphaticus (Tets over den status thymolymphaticus). Meursing (F.), Geneesk. Bl. Klin. en Lab. v. d. prakt. (Haarlem), 1921, **22**, 347-380.

A very good general review of the literature. The author found a remarkable number of large thymi in people who had come to accidental deaths. He denies that there is any relation between status thymicus and a narrow aorta.—J. K.

Exposure of the hyperplastic THYMUS to x-rays in myasthenia pseudoparalytica (Über die Röntgenbehandlung der hyperplastischen Thymus bei Myasthenia pseudoparalytica). Pierchalla (L.), Therap. Halbmonatsh. (Berlin), 1921, **35**, 504-505.

A woman of 48 with a typical myasthenia pseudoparalytica, with a normal **thyroid,** but a large thymus-shadow was treated by x-rays. The symptoms disappeared as did the myasthenic muscle reaction. This cannot be called a definite cure, however; there may be a remission. Nevertheless the patient has now for many months been able to do her work.—J. K.

THYROIDECTOMY under local anesthesia. Allen (C. W.), Am. J. Surg., Q. Suppl. Anesth. (N. Y.), 1921, **35**, 12-13.

A brief description of the author's technique for infiltration anesthesia in thyroidectomy, which he prefers in every case; regional anesthesia offers little advantage. It is pointed out that in removing the thyroid under local anesthesia it is preferable first to divide the isthmus to avoid the unpleasant choking sensation and increase the mobility of the two lobes.—C. R.

(THYROID) X-ray treatment of toxic goiter. Allison (R. G.), Beard (A. H.) & McKinley (G. A.), Am. J. Roentgenol. (N. Y.), 1921, **8**, 635-640.

In an exhaustive study of the x-ray treatment of toxic goiter the authors have given the following data and conclusions: Of the 27 cases of Graves' disease without complications, who were subjected to x-ray treatment, but were not operated upon, 24 are well, both from the clinical and laboratory standpoint. The treatment has been complete for nearly eight months. The remaining 3 cases came to operation. Of these three, one, they feel, was definitely improved before operation, the other two were normal a few months after operation. Of 6 cases of post-operative hyperthyroidism, which had relapsed, one showed a definite cure. The other 5 showed no

improvement. Of three cases of thyrotoxic adenoma none showed any responses to x-ray therapy. The only subject of the series who was operated upon during an increasing basal metabolic rate died an operative death. The results obtained in the earlier cases might have been attained more quickly if more intensive therapy had been used. No bad results or complications, which could be attributed to the treatment occurred in any of the series. Their experience with this treatment was convincing that only with the closest possible co-operation between the clinician and the roentgen therapist, can satisfactory results be obtained.—P. L. C.

Ten years of serum treatment for HYPERTHYROIDISM. Beebe (S. P.), Interstate M. J. (St. Louis), 1918, **25**, 161-171.

During the last ten years Beebe has treated some 4,000 cases of hyperthyroidism with antithyroid serum, the results being summarized in the present article. The author first answers certain theoretical and clinical criticisms which have been offered from time to time by various investigators. The results from, and the method of employing, antithyroid serum are quite different from the use of antidiphtheritic and antitetanic sera in the respective diseases. Antithyroid serum is the only therapeutic serum employed which is derived from injection of a human antigen. Its employment, therefore, requires great caution and must extend over a long period of time. Other therapeutic measures, such as rest, proper diet, etc., must accompany the use of the serum.—J. P. S.

THYROID disease and the war. Beebe (S. P.), Med. Rec. (N. Y.), 1918, **93**, 237-238.

The author anticipated a considerable increase in hyperthyroidism both among the soldiers and the civilians, as a result of the emotional crisis produced in action and by the nature of war. Fright, sudden danger such as soldiers encounter and profound grief and worry such as wives, mothers and sisters experience, naturally produce many instances of pathological thyroid activity. Beebe especially urges that proper provision for suitable treatment of such soldiers be made, pointing out that the general army hospital is not conducive to improvement or cure.—H. L.

Ten cases of THYROID disease. Beebe (S. P.), Med. Rec. (N. Y.), 1918, **93**, 705-711.

This is a report of nine cases of varying degrees of hyperthyroidism and of one case of carcinoma of the thyroid. The treatment of each patient is given in some detail.—J. P. S.

Malignant neoplasm of the THYROID with metastases in the intestine and bone. Binnie (J. F.), Surg., Gynec. & Obst. (Chicago), 1918, **26**, 288-291.

This is a report of a case of spindle cell sarcoma believed to have been primary in the thyroid gland. There were no clinical symptoms indicating interference with the function of this gland. The feature of greatest interest, because of the rarity with which it is encountered, was the metastasis in the intestine. Only two cases showing similar secondary tumors were found in 40 cases of sarcoma of the thyroid collected from the literature.—J. P. S.

Irregularity of neutralization consecutive to ablation of the THYROIDS and PARATHYROIDS (Déréglementation neutralisatrice consécutive a l'ablation des glandes thyroïdes et parathyroïdes). Bisgaard (A.), Hendriksen (V.) & Larsen (E. J.), Compt, rend. Soc. de biol. (Paris), 1921, **85**, 607-609.

Observations on two cases of tetania strumipriva and on a dog with total extirpation of the thyroids and parathyroids, support the theory that hypofunction of the parathyroids is an etiological factor in conditions of spasmophilia, notably tetany and idiopathic tetany. The conclusion is arrived at from a study of the N elimination.

—T. C. B.

(THYROID) The anesthesia problem in goiter surgery from the surgeon's standpoint. Blair (V. P.), Am. J. Surg., Q. Suppl. Anesth. (N. Y.), 1921, **35**, 5-6.

The author prefers local anesthesia upon patients showing marked hyperthyroidism with intoxication or degeneration in essential organs; in other cases he regards general ether anesthesia preferable to nitrous oxide.—C. R.

(THYROID) Notes sur le traitement chirurgical des goitres en Suisse. Block (J. C.) & Charrier (J.), Presse méd., 1921, **29**, 853-854.

Technical notes on Swiss methods of goiter surgery.—R. G. H.

(THYROID) Notes on the etiology of goiter (Note sur l'étiologie du goitre). Boitel (W.), Rev. méd. de la Suisse Rom. (Genève), 1920, **40**, 717-746.

Boitel comes to the conclusion that the distribution of goiter among the recruits in Switzerland does not agree with the zone described by Hunziker, namely, that corresponding to the climate in the regions between 600 and 1,000 meters, middle height (Abst. from Hunziker, Schweiz. med. Wchnschr., **51**, 337).—C. P. McC.

The effect of THYROID feeding on growth and organ-hypertrophy, in adult white rats. Cameron (A. T.) & Sedziak (F. A.), Am. J. Physiol. (Balt.), 1921, **58**, 7-13.

Thyroid was fed to adult white rats and the results showed a distinct retardation of growth. There was an actual gain in weight

of the **liver**, kidneys, heart, spleen, lymph glands and **adrenals**. The thyroids averaged a smaller weight. These results are in agreement with those found for young animals.—T. C. B.

The relation of the THYROID gland to the phenomena of immunity (Contribution a l'étude de l'action de la glande thyroïde sur les phénomènes d'immunité). Clevers (J.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 659-661.

The rôle of the thyroid in the processes of immunity has not been definitely established. Garibaldi thinks extirpation of the thyroid favors the production of hemolysin. Others find ablation of the gland has no effect. The author has tried to determine experimentally the effect of thyroidectomy on the production of antiovalbumin precipitin. He concludes that ablation of the thyroid favors the production of antibodies to ovalbumin.—T. C. B.

(THYROID) Experimental studies in a case of congenital myxedema (Experimentelle Untersuchungen an einem kongenitalen Myxödem). Cori (G.), Wien. klin. Wchnschr. (Vienna), 1921, **34**, 485-486. München med. Wchnschr., 1921, **69**, 1434.

Cori reviews the studies of Mansfield and Pap (Endocrinology, 1921, **5**, 520) on the heat-regulatory mechanism of thyroidectomized animals. The author then reports similar studies on a myxedematous child, 4 years of age. The temperature curves were studied, following immersion in a bath at 25° C. and in another at 40° C., both before and after thyroid feeding. Comparison of the temperature curves shows that in the untreated child the temperature fell to 33° C. in the cold bath and did not return to normal for 14 hours. Normal children showed an initial fall to 36° C. and the normal was regained after 1½ hours. After thyroid feeding the behavior of the myxedematous child was that of the normal. In the warm bath the myxedematous child did not react. There was no reddening of the skin, no sweating and no acceleration of the pulse or respiration. Following the parenteral injection of milk the child developed a typical protein fever with a temperature elevation to 39° C., that did not subside for 41 hours. The administration of thyroid increased the response of the child to adrenalin and atropin slightly, while it diminished the response to pilocarpin. The electrocardiogram described by Zondek as characteristic of myxedema (Endocrinology, 1921, **5**, 369) was also present in this case.—J. K.

Effect of the ingestion of THYROID on the male generative gland (Action de l'ingestion de corps thyroïde sur la glande germinative male). Courrier (R.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 484-486.

Observation and experimentation demonstrate that the thyroid hormone produces a trophic excitation of the genital glands. Cer-

tain authors, however, do not agree to this. Monteroso, for instance, claims that thyroid feeding causes degeneration of the seminal epithelium. His animals lost weight, and fasting we know causes genital atrophy. This was the problem. White rats were used, and care was taken to compensate for the increased metabolism by an abundant alimentation, sufficient to maintain a positive balance. Thyroid was fed in addition. A rat treated in this way for twenty-one days, during which time he took 75 grams of thyroid and increased in weight 30 grams, had perfectly normal testicles when examined histologically. Evidently when we avoid the effects of malnutrition, the thyroid does not cause degeneration of the testicle. Neither does the thyroid influence the maturation of the testicle; but after thyroidectomy the thyroid appears to exercise a trophic excitation of the testicle.—T. C. B.

Flagellated THYROID cells in the dogfish (Mustelus canis). Cowdry (E. V.), Anat. Record (Phila.), 1921, **22**, 289-299.

Flagellae are demonstrated by various methods in the thyroid gland of the dogfish. They are present without apparent adaptive value, but may have some bearing upon the problem of the ancestry of the gland, indicating perhaps its development from a flagellated epithelium like the endostyle of ascidians. The author holds that the presence of flagella shows that the primary direction of secretion is toward the follicular lumen, and not toward the peripheral blood vessels.—W. J. A.

(THYROID) Exophthalmic goiter in a girl of sixteen with special reference to etiology, and end results following ligation without thyroidectomy. Crance (A. M.), Am. J. Surg. (N. Y.), 1921, **35**, 9-12.

The etiology in the case reported was believed to be focal infections in teeth and tonsils. Improvement was marked after eradication of foci and ligations, but thyroidectomy was not permitted and the patient died, evidently from cardiorenal complications.—C. R.

Certain post-operative complications of operation on the THYROID gland. Crile (G. W.), Lower (W. E.), Sloan (H. G.) & Harrison (B. T.), Am. J. Surg. (N. Y.), 1921, **35**, 317-319.

Mention is made of possible attachment of scar-line to trachea, unevenness of neck contour, hoarseness resulting from trauma to nerves, temporary psychic aphonia, and other possible complications. The authors administer iodine in simple goiter for a year following operation to prevent rebuilding of the gland, and thyroid extract intermittently where thyroid deficiency is a complication.—C. R.

(THYROID) The anesthesia problem in goiter surgery. Crotti (A.), Am. J. Surg., Q. Suppl. Anesth. (N. Y.), 1921, **35**, 2-4.

A summary of the comparative merits of general and local anesthesia in thyroid surgery. The author prefers ether in most cases, but emphasizes the fact that hard and fast rules are impossible—that in goiter surgery the important secret of success is to know how to proportion the surgical act to the patient's condition. Failures from an injudicious operation should not be charged to anesthesia.—C. R.

THYROIDECTOMY—a brief review of 137 cases. De Courcy (J. L.), Am. J. Surg. (N. Y.), 1920, **34**, 282-285.

Observations are made from a series of 137 thyroidectomies with a very low mortality rate. It was noted that the most immediate and permanent results were obtained when both lobes and the isthmus were removed, it being suggested that single lobectomy and ligations are dangerous without being efficient in many cases. The fact is stressed that removal of foci of infection are but preliminary to removal of the diseased thyroid, the eradication of foci not being curative per se.—C. R.

(THYROID) Treatment of endemic goiter (Essai de traitement du goitre endémique). Degrais (P.), Progrès. méd. (Paris), 1921, **36**, 524-525.

Degrais believes that, on the whole, best results are to be obtained in endemic goiter by treatment primarily tonic. He relies upon sodium arsenate, strychnia, sodium glycerophosphate and quinine. This treatment, however, is not efficacious in adolescent goiter. He believes that drinking water does not play a major role in the etiology of endemic goiter, but that climatic conditions in general must be considered. Abrupt variations in meteorological conditions are regarded as of especial importance.—R. G. H.

Reactions of the liver cell of frog tadpoles to THYROID feeding (Divers aspects de la cellule hépatique chez les têtards de Rana temporaria nourris avec de la thyroïde). Dragoiu (J.) & Fauré-Fremiet (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 434-436.

The feeding of thyroid to tadpoles of Rana temporaria, after administration of **thymus**, or of thymus plus starch, produces definite changes in the nucleus and cytoplasm of the liver cells. In the nuclei minute vacuoles appear concerning the nature of which the author hesitates to make any suggestion. In the cytoplasm there is a marked development of so-called parasomes, which the author believes to be identical with similar structures described by Laguesse, Pacaut and Vigier in other cells. Each parasome consists of a central granule which is highly refractive and does not stain easily, surrounded by concentric lamellae. Sometimes they are double. A

single parasome may be larger even than the nucleus. The author remarks upon their absence in the pancreas and refrains from any statement of the functional significance of the parasomes.—E. V. C.

Histological study of the phenomena induced in the tadpoles of Rana temporaria by THYROID feeding (Étude histologique des phénomènes provoqués chez le têtard de Rana temporaria par l'alimentation thyroïdenne). Dragiou (J.) & Fauré-Fremiet (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 437-439.

A histological study of the accelerated metamorphosis induced by thyroid feeding.—T. C. B.

On the existence of evidence of direct continuity between PARA-THYROIDS, THYROIDS, and THYMUS nodules in mammalia (Sur l'existence de rapports de continuité directe entre parathyroïdes, thyroïde et nodules thymiques chez les mammifères). Dustin (A. P.) & Gérard (P.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 876-877.

Histological.—T. C. B.

Anomalies of THYROID function as related to gestation (Des anomalies de la fonction thyroïdienne dans leurs rapports avec la gestation). Fruhinsholz (A.) & Parisot (J.), Gynéc. et Obst. (Paris), 1921, **4**, 169-206.

An extensive and well written review of the subject. The provisional conclusions of the study are as follows: Gestation seems to determine a state of physiological compensatory hyperthyroidism which is more marked in the second period of pregnancy. This hyperactivity may become pathological and may manifest itself at different stages of pregnancy. Sometimes it does not appear until delivery, just as if it had been maintained in a state of neutralization by the condition of pregnancy. Hyperthyroidism is probably not favorable to fecundation. When that condition is present before gestation, there often results a diminution of activity, although in exceptional cases an exacerbation may occur. Hypothyroidism is more favorable to fecundation. When gestation is in progress the hypothyroid condition may be improved if the status is mild; if low, it may be aggravated. There is certainly a relation between tetany and pregnancy, and between tetany and **parathyroid** insufficiency. Certain offspring of mothers having thyroid disturbances have a predisposition to glandular troubles which are not necessarily homologous to those of the mother.—F. S. H.

The production of heat in tadpoles fed THYROID or THYMUS (La produzione di calore nei girini alimentati con tiroide o con timo). Gayda (T.), Arch. di Fisiol. (Florence), 1921, **19**, 267-285.

Tadpoles of Bufo vulgaris, fed with thyroid and showing the phenomena of acceleration of metamorphosis and arrest of growth, exhibit a heat-production which, referred to unit body-weight, is distinctly greater than that of tadpoles of the same age and under the same temperature conditions (15° C.), but fed with flesh. The fact is more evident when the tadpoles are kept at a somewhat higher temperature (22.5° C.), under the precise conditions which produce greatest thyroid effect on metamorphosis. When, with protracted feeding, the tadpoles tend to remain immobile and cease feeding, the production of heat diminishes progressively yet remains greater than with the flesh-fed tadpoles. Bufo tadpoles fed thymus, and exhibiting slight acceleration of growth and retardation of metamorphosis, show a heat production but little greater than that of controls fed flesh.—A. T. C.

(THYROID) A new method for the determination of the fibrin percentage in blood and plasma. Gram (H. C.), J. Biol. Chem. (Balt.), 1921, **49**, 279-295.

The percentage of fibrin in both plasma and whole blood was found to be higher in one case of Graves' disease than in normal. —F. S. H.

(THYROID) Skin rashes in exophthalmic goiter. Gundrum (F. F.), Cal. State J. Med. (San Francisco), 1921, **19**, 339.

The author reviews the literature on skin rashes associated with exophthalmic goiter and notes that the majority of authors have merely described the rashes without undertaking to connect them with physiological effects of hyperthyroidism. Hyde and McEwen in the Amer. J. Med. Science, June, 1903, attempted a classification into three groups; first, dermatoses of accidental concurrence; second, more or less distantly related to the essential morbid processes of goiter, and third, intimately related to the pathology of goiter. A large majority of patients having skin rashes and exophthalmic goiter have belonged within the first or second group. Indeed, it is likely that most of the skin troubles are no more than the results of hypersusceptibility to injury of the moist, congested and often slightly edematous skin. Gundrum reports two cases in which a definite dependence of the rash upon thyroid overactivity seemed to obtain. They were characterized by discreet, deep pink, macules barely perceptibly raised, varying from the size of a pea to that of a quarter. They disappeared on pressure. Itching was intense. There was no scaling, weeping, or edema. In both cases, partial thyroidectomy was done. Upon the first postoperative day, a marked exacerbation of the rash occured followed within the fourth day by a complete subsidence without return.

—Author's Abstract.

(THYROID) Basal metabolism and its clinical application. Hepburn (J. S.) & Eberhard (H. M.), J. Am. Inst. Homeop. (N. York), 1921, **14**, 231-237.

The various methods for the determination of basal metabolism are described, and results obtained with the metabolimeter of Jones are reported. A case of hypothyroidism with a basal metabolic rate of —16.3% was restored to a normal rate by administration of desiccated **thyroid.** A case of hyperthyroidism had a rate of +35.4% after operation on the thyroid. Two weeks after x-ray treatment the rate had risen to +58.7%; and it decreased to +35.4% at the end of another week. A second x-ray treatment was then given; 1 week later the rate was +45.7%; at the end of a further period of 2 weeks it had decreased to +17%. Hence exposure of the thyroid to the x-ray produced first an increase, then a gradual decrease in the basal metabolic rate.—Chem. Abst., **15**, 3868.

Accelerated development of tadpoles after feeding with THYROID (Tets over de versnelde ontwikkeling van kikkerlarven onder den infloed van voeding met gl. thyroidea). Heringa (G. C.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1921, **65**, (II.), 1930-1934.

When thyroid is given to tadpoles metamorphosis is accelerated. If the region of the gills in control animals is compared to the same region in animals fed with thyroid it is found that the latter do not show typical epithelium. This epithelium, which is possessed of a glandular function, becomes atrophic in animals fed with thyroid. While thyroid feeding apparently accelerates metamorphosis the actual differentiation of the tissues is retarded. At a time when the control animal already has adult muscles the thyroid animal still has embryonal muscular tissue. The author compares these findings to those of Walter, who states that if after thyroidectomy a nerve is cut, neither degeneration nor regeneration of the nerve is seen.—J. K.

Concerning chemical heat regulation in THYROID-less rats (Über die chemische Wärmeregulation schilddrüsenloser Ratten). Hildebrandt (F.), Arch. f. exper. Path. u. Pharmakol. (Leipzig), 1921, **90**, 330-335.

Hildebrandt controverts the statement that the thyroid is of great importance in temperature regulation. He denies the presence of any difference as regards chemical heat regulation in normal and thyroidless rats.—W. J. A.

(THYROID) Modern surgical treatment of goiter (Ueber den gegenwärtigen Stand der operativen Behandlung des Kropfes). Hildebrand (O.), Deutsche med. Wchnschr. (Berlin), 1922, **48**, 16-17. Of technical interest.—J. K.

The THYROID question (Zur Kropffrage). Hotz (G.), Schweiz. med. Wchnschr. (Basle), 1921, **51**, 1153-1155.

Hotz points out that thyroid prophylaxis for children is a pressing necessity in his country and should be carried out on an extensive scale with governmental assistance. The writer describes the types in which iodides as prophylactic agents are beneficial and those in which harmful results are to be anticipated. The principal field for prophylaxis is in young children, especially among girls. In school children massive doses of iodides are not essential. In many instances goiters exist among all children of given families, the condition depending upon the state of thyroid function of the parent during pregnancy. Among older women, especially the hard working class, goiters are very prevalent and are associated with premature age. In such types the iodides are said to be very harmful, resulting in a depletion of body strength and the production of an artificial Basedow's disease. For such conditions partial bilateral thyroidectomy yields better results. Specific cases of the several types are included in the article.—C. P. McC.

Sensitivity of THYROIDECTOMIZED animals to diphtheria bacilli and toxin (Sensibilité des animaux éthyroïdés envers les toxines et le Bacille diphterique). Houssay (B. A.) & Sordelli (A.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 677-678.

A brief note giving the results of many experiments. Thyroidectomized guinea pigs and rabbits have the same resistance as normal animals, except in the period of enfeeblement and cachexia, when the resistance diminishes.—T. C. B.

Formation of antibodies in THYROIDECTOMIZED animals (Formation d'anticorps chez les animaux éthyroïdés). Houssay (B. A.) & Sordelli (A.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 679-680.

A study of the production of antibodies in the rabbit, dog and horse, deprived of their thyroids. Various antigens were used. The results are difficult to explain and a general conclusion cannot be drawn. Thyroidectomy has no influence on the production of hemolysins and agglutinins. The case of antitoxin is complex. In the thyroidectomized rabbit and especially the horse, the production of diphtheria and tetanus antitoxin is feebler than in the controls; in the dog, on the contrary, it is better than in the controls. It will be necessary to ascertain if the difference is due to distinct diet, or to qualitative or quantitative differences in the protein ingested. It is also possible that extirpation of the thyroid modifies the skin or other organs, and thus influences the production of antitoxin.

THYROIDECTOMY in cattle (La thyroïdectomie chez les bovins). Hug (E.), Compt. rend. Soc. de biol. (Paris), 1921, **85**, 953-954.

The thyroid was removed from 3 calves, two at the age of 2 months, and one at the age of 3 months. No symptoms were observed except a retardation of growth; they were inferior to the controls of the same age and race (short horns) in size and weight. The calcium of the blood was the same as in the controls. They were observed during 19 months.—T. C. B.

(THYROID) The dependence of goiter incidence among recruits upon the median yearly temperature (Über die Abhängigkeit des Kropfvorkommens bei Rekruten von der mittleren Jahrestemperatur). Hunziker (H.), Schweiz. med. Wchnschr. (Basel), 1921, **51**, 337-343.

Hunziker in this publication extends his observation that goiter among army recruits is related to the variation of temperature in the various Swiss districts. Observations to the number of 1,235 were made in one series of 95 districts, and 247 distributed over 19 other separated districts. Investigations were made as to the effect of elevation, temperature, wind conditions, cloudiness, humidity, etc. Extensive tables are included by the author supplying precise data concerning these several investigations. No relation was established between goiter and cloudiness or barometric reading, but a definite relation was found between temperature and goiter and a less distinct relation between humidity and goiter. With reference to temperature Hunziker states that disabling goiter among recruits, as observed during the past thirteen years, was distributed over the country in a manner dependent upon the median annual temperature of the various districts. For northern Switzerland this is 7° C.—C. P. McC.

Diagnosis of hypothyroidism. Janney (N. W.), Cal. State J. Med., 1921, **19**, 313.

This article emphasizes the exact correlation of laboratory data with often inconspicuous clinical symptoms and signs necessary for the detection of latent cases of hypothyroidism. (See report in full "Concerning the Diagnosis and Treatment of Hypothyroidism,") N. W. Janney, M. D., and H. E. Henderson, M. D., Santa Barbara, Cal., Arch. of Int. Med. (Chicago), 1920, **26**, 297-318. The frequency of latent hypothyroidism is emphasized and the infrequency of typical myxedema and cretinism. Hypothyroidism may present clinical symptoms resembling neurasthenia, intestinal toxemia, arterio-sclerosis, the greatest aid to exact diagnosis and treatment being determinations of the metabolic rate.

The relation of the THYROID to irregularities of metamorphosis in amphibia. Jensen (C. O.), Publication of the Royal Vet. & Agricult. Serum Laborat. (Copenhagen), 1921, **72**, 145-171.

(Danish with English summary.) The thyroid of axolotl (Amblystoma mexicanum) was studied before and after the period at which metamorphosis may occasionally take place in this form. The gland is not abnormal in early stages, but when the animal is six to nine months old, regressive changes take place in it. These are like the senile changes seen in the thyroids of old specimens of Amblystoma punctatum, and consist of epithelial atrophy with coalescence of neighboring follicles. Five cases of precocious metamorphosis have been observed by this author among larvae of Bufo and Rana. In two of these the thyroids were unusually large, while in the other three no hypertrophy of the gland was observed. The author gives no measurements of these precocious frogs, but the plates suggest that they are abnormally small, and it is possible that the thyroids were large in proportion to the size of the animals. In wintering larvae of R. esculenta, the follicles of the thyroids are considerably distended by colloid, and the epithelium is flattened. In giant larvae very large thyroids are found, but here again the author has not considered the abnormal size of the animals. The data presented are not sufficient to throw any great light on the relation of the thyroid to precocious or delayed metamorphosis except in the case of the axolotl.—M. M. H.

(THYROID) Partial metamorphosis in Amblystoma mexicanum. Jensen (C. O.), Publication of the Royal Vet. & Agricult. Serum Laborat. (Copenhagen), 1921, **74**, 173-180; Compt. rend. Soc. de biol. (Paris), 1921, **84**, 423-424.

Intra-abdominal injection of iodocasein in an axolotl about three years old produced a partial metamorphosis. The resultant "demi-amblystoma" is like the adult form in shape, and in the character of the skin and eyelids. It has the tail, webbed feet, gill clefts and internal gill apparatus and the mouth of the larva.—M. M. H.

The THYROID gland and anomalies of metamorphosis in the Anura (La glande thyrôide et les anomalies de métamorphose chez les Anoures). Jensen (C. O.), Compt. rend. Soc. de biol. (Paris), 1921, **84**, 948-949.

Same data as those presented in the Danish paper already reviewed, without the plates.—M. M. H.

THYROID feeding of invertebrates (Ueber Schilddrüsenfütterung an Wirbellosen). Kahn (R. H.), Arch. f. d. ges. Physiol. (Berlin), 1921, **192**, 81-92.

From experiments on the larvae of Corethra plumicornis, Ecdyurus forcipula, and Tenebrio molitor, it is concluded that the characteristic actions on growth and differentiation produced by thyroid feeding on tadpoles are not produced in invertebrates.

—A. T. C.

A striking case of asymmetry in the THYROID region associated with the occurrence of a branchial cyst. Kampmeier (O. F.), Anat. Record (Phila.), 1921, **22**, 311-316.

In an adult negro male it was discovered upon dissection that the left lobe of the thyroid and the isthmus were entirely lacking. The right side was normal. Associated with the absence of the left lobe, a cyst, apparently of branchial origin, was present.—W. J. A.

(THYROID) Treatment of goiter (Behandlung des Kropfes). Krecke (A.), München. med. Wchnschr., 1921, **68**, 1429-1430.

Often the best effect is seen from sending a patient to a place free from goiter or from changing the origin of his drinking water. Some kinds of diffuse goiters, especially in young girls, decrease in size when iodine is given. In elderly people it is necessary to be careful with iodine, for it may cause loss of flesh and even Graves' disease. When a patient complains of palpitations the administration of iodine must be stopped at once. The same must be said of the administration of thyroid. The author warns against the use of iodine ointments or x-rays, which both cause adhesions. Operation is necessary when there are symptoms of thyrotoxicosis or when respiration becomes difficult. In recent years mortality is somewhat higher than formerly because instead of a hemi-strumectomy the operation is performed on both sides. The greatest dangers are tetany and paralysis of the nervus recurrens. Contraindications are serious diseases of respiration or circulation. Recurrences after operation are not rare.—J. K.

(THYROID) Ether-oil colonic anesthesia in goiter surgery. Lathrop (M.), Am. J. Surg., Q. Suppl. Anesth. (N. Y.), 1921, **35**, 14-16.

Attention is called to the fact that subjects of hyperthyroidism may be anesthetized in bed without apprehension or upset through the use of colonic injection of olive oil, ether, and paraldehyde (Gwathney) reinforced if desired by local anesthesia. Favorable results in several hundred cases are reported.—C. R.

(THYROID) Colloid goiter. Latzel (R.), Deutsche med. Wchschr. (Berlin), 1921, **47**, 1282.

Demonstration of a woman of 21, with a positive venous pulse and a colloid goiter. Probably the goiter is situated between the jugular and subclavian veins and the large arteries, thus transmitting to the former the pulse of the latter.—J. K.

(THYROID) Observations on certain types of toxic goiter. Levinson (C. G.), Am. J. Surg. (N. Y.), 1917, **31**, 234-240.

Several case reports illustrative of improvement after surgical intervention in thyrotoxicosis. The author believes that exophthalmic goiter is always a surgical disease.—C. R.

THYROID conservation after goiter operations (Zur Stumpfversorgung bei Kropfoperationen). Liek (E.), Zentralbl. f. Chir. (Leipzig), 1921, **48**, 1656-1658.

Of technical surgical interest.—J. K.

Studies on compensatory hypertrophy of the THYROID gland. Loeb (L.), J. M. Research (Boston), 1919, **40**, 199-228.

Previous investigators in this field have used dogs. Loeb believes that dogs are too susceptible to hypertrophies of the thyroid gland to permit accurate conclusions. In the experiments reported in this paper, he therefore, used guinea pigs as the experimental animals. Loeb first made a careful study of the normal histology of the thyroid of the guinea pig, and describes it in detail. He found that removal of from one-half to three-fourths of the entire thyroid gland did not result in hypertrophy of the remaining gland tissue. After almost complete removal of the thyroid there was hypertrophy of the small fragments that had been left behind. The histologic changes observed in these remnants are described fully. Almost complete extirpation of the thyroid in a pregnant guinea pig need not interrupt the pregnancy, but in most cases the compensatory hypertrophy of the remaining gland tissue was retarded. Complete thyroidectomy during pregnancy or before fertilization did not induce hypertrophy of the thyroid gland of the offspring.

—J. P. S.

Studies in Compensatory Hypertrophy of the THYROID Gland. II. (a) Hypertrophy in auto-transplants of the thyroid gland. (b) Does a deficiency in organ function influence transplantability? (c) Hypertrophy in multiple transplants of the thyroid gland. Loeb (L.), & Hesselberg (C.), J. M. Research (Boston), 1919, **40**, 265-288.

In a large majority of cases conditions in the autotransplant and remnant of the extirpated gland are identical; in a few instances the hypertrophy is less marked in the autotransplants. In remnants as well as in autotransplants, three periods, differing in the character of proliferation can be distinguished: (a) the period of regenerative proliferation; (b) the period of proliferation due to early hypertrophy; and (c) the resting period. A deficiency in functionally (metabolically) active tissues does not noticeably influence the processes in organization and especially in vascularization which determine the healing-in of the graft. Compensatory hypertrophy may, however, secondarily cause an enlargement of the blood vessels which supply the hypertrophic area. The grafted lobes of thyroid in cases of multiple transplantations have the same fate as the corresponding tissue in cases of single transplantations; and the success of the transplantation does not depend upon the physio-

logic need in the organism of the specific function supplied by the transplanted tissue.—J. P. S.

Studies on Compensatory Hypertrophy of the THYROID Gland. III. (a) The Effect of homoiotoxins on hypertrophy of the thyroid. (b) Change in weight of the host as a factor in compensatory hypertrophy. (c) Phagocytosis in hypertrophic thyroid gland. Loeb (L.), & Hesselberg (C.), J. M. Research (Boston), 1920, **41**, 283-303.

A. After homoiotransplantation of the thyroid gland following an almost complete extirpation of the thyroid host, hypertrophy of the transplant may occur. The frequency and in some cases also perhaps, the intensity of the hypertrophic changes are probably diminished in cases of homoiotransplantation as compared to autotransplantation. A mitotic proliferation is associated with the development of hypertrohpy in the homoiotransplanted as well as in the autotransplanted glands. The authors believe that the results obtained are due to the interaction of two substances, (1) the growth substances calling forth hypertrophy of the thyroid gland, and (2) homoiotoxins. These growth substances are not individual-specific, which is in accordance with the fact that hormones in general are not only not individual-specific, but not even species-specific. In general, the authors conclude, homoiotoxins affect injuriously not only the ordinary regenerative reaction, such as we observe after transplantation, but that they likewise interfere in an unfavorable manner with the action of various growth substances, without, however, being able to overcome the latter entirely.

B. The Authors advance the tentative conclusion that the occurrence of hypertrophy is usually associated with a greater gain in weight than lack of hypertrophy, and, conversely, that a gain in weight of the animals in which a great part of the thyroid had been extirpated is a factor more favorable for the development of hypertrophy than a loss of weight.

C. After injury of the thyroid gland, particles of blood pigment may appear in the acinus cells as well as in phagocytes which are found in the lumen of the acini. These granules seem to persist longer in the acinus cells than in the lumen of the acini; they are especially prone to appear in hypertrophic cells; they are never seen in normal glands. The authors conclude that in this case they have to deal with phagocytic activity on the part of thyroid cells.

—J. P. S.

Studies in compensatory hypertrophy of the THYROID gland. IV. The influence of iodine on hypertrophy of the thyroid gland. Loeb (L.), J. M. Research (Boston), 1920, **41**, 481-494.

Loeb extirpated a quantity of thyroid gland in guinea pigs necessary to call forth compensatory hypertrophy. To the animals so

treated he gave iodine, either potassium iodide by mouth or subcutaneously, or iodine dissolved in sesame oil. He found indications that perhaps iodine preparations increase the hypertrophic changes occurring in the remnants of the gland. But Loeb admits that this cannot be stated definitely at the present time. It is rather contrary to the prevailing views in regard to the effect of iodine upon hypertrophy of the thyroid. The author's results also suggest that summer heat may be a factor which interferes with compensatory hypertrophy.—J. P. S.

Studies on compensatory hypertrophy of the THYROID gland. V. The effect of the administration of thyroid, THYMUS gland and tethelin and of a meat diet on hypertrophy of the thyroid gland in guinea pigs. Loeb (L.), J. M. Research (Boston), 1920, **42**, 77-89.

Feeding guinea pigs with thyroid tablets greatly inhibits compensatory hypertrophy of the thyroid gland in guinea pigs.—J .P. S. almost complete thyroidectomy. This effect is direct and specfic, and is not due to the loss of weight induced by the feeding of the thyroid. Preparations of iodine given along with the thyroid did not counteract the effect of the tablets. Feeding the thymus gland did not prevent hypertrophy of the thyroid remnants. Repeated injections of **tethelin** did not noticeably influence the degree of hypertrophy of the thyroid remnants which follows almost complete thyroidectomy. A diet consisting chiefly, but not exclusively of meat did not produce hypertrophic changes in the thyroid gland; such a meat diet neither prevented nor noticeably increased compensatory hypertrophy of the thyroid gland in guinea pigs.

(THYROID) On differences in the results of various kinds of syngenesioplastic transplantations in dependence upon the relationship between donor and host. Loeb (L.), J. M. Research (Boston), 1920, **41**, 305-325.

Loeb studied the results of transplanting thyroid gland from mother to child, from child to mother and to brother or sister. Following transplantations two reactions take place; first, fibroblastic and vascular, and second, lymphocytic. These reactions appear to be the result of the formation of syngenesiotoxins. These toxins, and the reactions which they stimulate, are strongest after transplantations from child to mother and weakest after transplantations to brother or sister, while transplantations from mother to child occupy an intermediate position. Loeb thinks that these experimental results may have a practical value in the selection of a donor for tissue grafting.—J. P. S.

(THYROID) Treatment of Graves' disease with iodine (Morbus Basedowii und Jodtherapie). Loewy (A) & Zondek (A.), Deutsche med. Wchnschr. (Berlin), 1921, **47**, 1387-1389.

Neiszer some time ago reported good results from very small doses of iodine in Graves' disease. Loewy and Zondek tried very small doses of KI with most brilliant success. The subjective feelings of the patients improve and they gained in weight. By studying the respiratory quotient they could prove that the intensity and rapidity of metabolism is largely diminished by this treatment. They advise to begin with 3 drops of a 5% solution of KI, three times daily and to increase the dose gradually until the patient complains of feeling worse again or till he begins to lose flesh when a smaller dose must be given.—J. K.

(THYROID) The value of anociation in goiter operations. Lower (W. E.), Am. J. Surg., Q. Suppl. Anesth. (N. Y.), 1921, **35**, 7-9.

A brief exposition of "anoci-association" in thyroid surgery, including elimination of the patient's apprehension, narcotics before operation, nitrous oxide inhalation and local anesthesia to prevent apparent impulses reaching the brain. Preliminary ligation is urged as a general procedure.—C. R.

Carcinoma of the THYROID. McWilliams (C. A.), Ann. Surg. (Phila.), 1917, **65**, 787.

Report of an alleged instance of carcinoma of the thyroid gland in a girl 18 years of age; it had been present three years. Surgical removal was followed by recovery. There were no symptoms of hyperthyroidism.—J. P. S.

(THYROID) Colloid goiter. Morf (P. F.), Surg. Gyn. and Obst. (Chicago), 1918, **26**, 360.

Not of endocrine interest.—E. N.

Tuberculosis of the THYROID. Mosiman (R. E.), Surg. Gyn. & Obst. (Chicago), 1917, **24**, 680-693. 4 photomicrographs.

This article is a report of 9 cases of tuberculosis of the thyroid. Most of them were discovered accidentally in course of the routine microscopic examination of glands removed at operation. In all of these cases there was evidence of a primary focus of tuberculosis in some other part of the body, or a definite history of a prolonged exposure to the disease. The author therefore believes it is extremely doubtful if primary tuberculosis of the thyroid occurs. The tuberculous process was found associated with various physiological and pathological changes in the gland such as hyperplasia, pure colloid goiter, adenomatous goiters, and sarcomas.—J. P. S.

A case of woody THYROIDITIS. Nicholson (Daniel), Jour Can. Med. Assoc. (Toronto), 1921, **11**, 742-743.

A woman, 38 years old, previously always well, suddenly developed severe headaches, chills, nightsweats and anorexia with pain in the thyroid region and a pulse of 160. She showed none of the classical eye symptoms of Graves' disease, but she had fine digital tremors. There was bilateral enlargement of the thyroid, each lobe being about the size of a hen's egg, very hard and easily defined. Carcinoma of the thyroid was diagnosed and the mass removed. The tumor consisted of very dense fibrous tissue stroma with yellowish areas at intervals, and a few cysts. Microscopically there was a typical picture of tuberculous granulation tissue. Fibrous elements predominated, clusters of round cells were seen, giant cells were very numerous, but there was no caseation. Many of the colloid spaces were destroyed. The pathological findings would seem to be of longer duration than could be accounted for by the patient's symptoms. The prognosis in this condition is excellent. Illustrated by half tone plate of a microscopic section.
—Author's Abst.

(THYROID) Relation between the chloride content of the blood and its volume per cent of cells. Norgaard (A.) & Gram (H. C.), J. Biol. Chem. (Balt.),.1921, **49**, 263-278.

Chloride content of blood corpuscles is nearly constant at 0.31 per cent. Plasma values are also constant at close to 0.61 per cent by the method described. The figures in cases of goiter do not differ from the normal.—F. S. H.

The quantity of glycogen in the liver and muscles of THYROPARATHYROIDECTOMIZED animals (Sur la teneur en glycogéne du foie et des muscles chez les animaux thyroparathyroïdectomisés). Parhon (M.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 140-142.

We know from the work of others that there is a diminished assimilation of glucose in parathyroidectomized animals; but these results have been obtained by determining the sugar in the urine after the injection of glucose. The present paper deals with the amount of glycogen in the liver and muscles of thyroparathyroidectomized dogs, fed on known quantities of bread per kilo of body weight. Tables of results are given. From the tables it is evident that the liver and muscles of the experimental animals contain less glycogen than the normal controls; the diminution is much greater in the liver than in the muscles, because the liver furnishes the carbohydrate necessary for muscular energy. The parathyroid secretion restrains the consumption of carbohydrates in the organism, probably by diminishing the excitability of the muscles. It must have an important role in muscle tonus, for when it is absent carbohydrates are used in excess and muscle tonus profoundly disturbed.
—T. C. B.

(THYROID) Prophylaxis of goiter (Prophylaxie du goitre). Roux (C.), Rev. méd. de la Suisse Rom. (Geneva), 1918, **38**, 317-321.

The paper is a plea for the prophylactic use of iodine as well as its therapeutic use. It is pointed out that while the etiology of goiter is unknown, there is now no question that the immediate cause of thyroid hyperplasia is an iodine deficiency. He also shows that there are no serious dangers from the minute doses that are needed and have been used in goiter prevention.—D. M.

(THYROID) Struma maligna. Schädel, München. med. Wchnschr., 1921, **68**, 1506.

The author observed 15 malignant out of 450 goiters seen in clinics. In his private practice he saw 4 malignant cases. Of these 19, 14 were cancer, 4 sarcoma, 1 sarcocarcinoma. Malignant goiter nearly always begins as benign. The first symptoms of malignant degeneration are increased size and consistence, decreased movability and neuralgiform pains. Though the prognosis is very bad, the best results are obtained with x-ray treatment followed by operation. Malignant goiters almost never produce symptoms of hyperthyroidism.—J. K.

(THYROID) The sympathicus theory of Graves' disease (Zur Sympathicus theorie des Morbus Basedowi). Seitz (E.), Zentralbl. f. inn. Med. (Leipzig), 1921, **42**, 842-844.

In studying the amount of blood sugar and its variations in Graves' disease the author comes to the conclusion that in diseases of the thyroid there exists often an increased irritability of the sympathicus. This is most marked in Graves' disease. A fortnight after the operation for Graves' disease the blood sugar and the tonus of the vegetative nervous system is normal. In some cases of colloid goiter, however, the sympathicotonia may be increased after the operation. As there are cases of Graves' disease without a disturbed function of the sympathicus Seitz believes that this disease has its primary seat in the thyroid. The study of the blood sugar is a good way to get information concerning the seriousness of the disorder. Surgical treatment of Graves' disease gives splendid results.—J. K.

(THYROID) Genesis of congenital infantile myxedema (Zur Genese des angeborene und infantilen Myxödems). Siegert, München. med. Wchnschr., 1921, **68**, 997.

It is possible that the anlage of the thyroid degenerates or that the normal organ undergoes degeneration. It has never been proved that there exist cases without an anlage of the thyroid.—J. K.

Clinical observations on 100 nitrous oxid-oxygen anesthesia in cases of HYPERTHYROIDISM. Sise (L. F.), Am. J. Surg., Q. Suppl. Anesth. (N. Y.), 1921, **35**, 9-12.

The author states that the addition of nitrous oxid-oxygen anesthesia to local anesthesia with preliminary narcosis reduced the incidence of shock, lowered respiration and pulse rate during a series of 100 thyroidectomies by Lehey, and he believes made post-operative thyroid "storm" less severe. A three per cent mortality is reported.—C. R.

(THYROID) A case of hypothyrosis with symptoms resembling urticaria (Ein Fall von Hypothyreose mit urtikariaähulichen Erscheinungen). Stemmer, München. med. Wchnschr., 1921, **68,** 1405-1406.

A woman of 22 suddenly showed a reddening and a swelling of the skin and mucous membranes. **Hypophysis, ovary** and **adrenal** substance were given without success. The sexual organs were hypoplastic. Thyroid gave good results.—J. K.

(THYROID) Nonthyrotoxic goiter. Slesinger (E. G.), Practitioner (Lond.), 1921, **57,** 355-366.

The following elaborate classifications is introduced and upon it is based a clinical dissertation of considerable interest:

Innocent Goiter

1. Parenchymatous goiter
   - Physiological
   - Toxic
   - Congenital
   - Acquired
2. Colloid goiter
   - Adenoma
   - Diffuse
   - Diffuse adenomatous
   - Cystic
   - Fibrous
   - Calcareous
   - Osseous
3. Foetal adenoma
4. Hyperplastic thyrotoxic goiter (Graves' disease).

Malignant Goiter

1. Epithelial tumours
   - Carcinoma
   - Malignant adenoma
   - Metastatic colloid goiter
   - Parastruma
   - Postbranchial goiter
   - Papilloma
   - Cancroid

2. Connective tissue tumours
   Sarcomata
   Endotheliomata
   Peritheliomata.

Each of the above types is then described. The various pressure signs and symptoms are excellently reviewed. Finally the prophylactic surgery of long standing goiters in order to prevent malignancy is emphasized, especially in view of the almost invariably fatal prognosis when malignancy has once definitely begun. —H. L.

(THYROID) "Forme fruste" der Myxödem. Stransky (E.), Wiener klin. Wchnschr., 1921, **34**, 575.

Demonstration of a patient with a swollen face, thin hair, fragile nails, normal temperature and palpable thyroid. Now and then migraine-like headaches are experienced. Psychically the patient is dull, with now and then intervals in which she is very bright. She has been five times pregnant. The author considers this case as hypothyroidism.—J. K.

(THYROID) Congenital myxedema (Myxœdema congenital). Talliens, Rev. méd. de la Suisse Rom. (Geneva), 1918, **38**, 268.

This paper reports the case of an infant, aged five months, with the typical appearance of a myxedematous cretin. Skin thick and dry; tongue large; abdomen distended; umbilical hernia; hands and feet short and square; thyroid not palpable. At first the patient was treated with "panglandine" with little success; later desiccated thyroid 0.15 to 0.3 grams daily was given with good results both as regards physical and mental development.—D. M.

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